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(54) Titre: ANTIGENES DE STREPTOCOCCUS (54) Title: STREPTOCOCCUS ANTIGENS

(57) Abrégé/Abstract:

Streptococcus proteins and polynucleotides encoding them are disclosed. Said proteins are antigenic and therefore useful vaccine components for the prophylaxis or therapy of streptococcus infection in animals. Also disclosed are recombinant methods of producing the protein antigens as well as diagnostic assays for detecting streptococcus bacterial infection.





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										I 86% S 90%		BVH11-2 P4241 BVH11

(57) Abstract

Streptococcus proteins and polynucleotides encoding them are disclosed. Said proteins are antigenic and therefore useful vaccine components for the prophylaxis or therapy of streptococcus infection in animals. Also disclosed are recombinant methods of producing the protein antigens as well as diagnostic assays for detecting streptococcus bacterial infection.

NOVEL STREPTOCOCCUS ANTIGENS

FIELD OF THE INVENTION

5 The present invention is related to antigens, more particularly protein antigens of streptococcus pneumoniaepathogen which are useful as vaccine components for therapy and/or prophylaxis.

10 BACKGROUND OF THE INVENTION

- S. pneumoniae is an important agent of disease in man especially among infants, the elderly and immunocompromised persons. It is a bacterium frequently isolated from
- 15 patients with invasive diseases such as bacteraemia/septicaemia, pneumonia, meningitis with high morbidity and mortality throughout the world. Even with appropriate antibiotic therapy, pneumococcal infections still result in many deaths. Although the advent of
- antimicrobial drugs has reduced the overall mortality from pneumococcal disease, the presence of resistant pneumococcal organisms has become a major problem in the world today. Effective pneumococcal vaccines could have a major impact on the morbidity and mortality associated with <u>S. pneumoniae</u>
- 25 disease. Such vaccines would also potentially be useful to prevent otitis media in infants and young children.

Efforts to develop a pneumococcal vaccine have generally concentrated on generating immune responses to the pneumococcal capsular polysaccharide. More than 80 pneumococcal capsular serotypes have been identified on the basis of antigenic differences. The currently available pneumococcal vaccine, comprising 23 capsular polysaccharides

that most frequently caused disease, has significant shortcomings related primarily to the poor immunogenicity of some capsular polysaccharides, the diversity of the serotypes and the differences in the distribution of serotypes over time, geographic areas and age groups. particular, the failure of existing vaccines and capsular conjugate vaccines currently in development to protect young children against all serotypes spurres evaluation of other S. pneumoniae components. Although immunogenicity of 10 capsular polysaccharides can be improved, serotype specificity will still represent a major limitation of polysaccharide-based vaccines. The use of a antigenically conserved immunogenic pneumococcal protein antigen, either by itself or in combination with additional components, 15 offers the possibility of a protein-based pneumococcal vaccine.

PCT Publication number WO98/18930 published may 7 1998 entitled "Streptococcus Pneumoniae antigens and vaccines" describes certain polypeptides which are claimed to be antigenic. However, no biological activity of these polypeptides is reported.

Therefore their remains an unmet need for Streptococcus

25 antigens that may be used as vaccine components for the
prophylaxis and/or therapy of Streptococcus infection.

SUMMARY OF THE INVENTION

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55

to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

In other aspects, there are provided vectors comprising polynucleotides of the invention operably linked to an expression control region, as well as host cells transfected with said vectors and methods of producing polypeptides comprising culturing said host cells under conditions suitable for expression.

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In yet another aspect, there are provided novel polypeptides encoded by polynucleotides of the invention.

15 BRIEF DESCRIPTION OF THE DRAWINGS

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Figure 1 is the DNA sequence of BVH-3 gene; SEQ ID NO: 1.

Figure 2 is the amino acid sequence of BVH-3 protein; SEQ ID 20 NO: 2.

Figure 3 is the DNA sequence of BVH-11 gene; SEQ ID NO: 3.

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Figure 4 is the amino acid sequence of BVH-11 protein; SEQ 25 ID NO: 4.

Figure 5 is the DNA sequence of BVH-28 gene; SEQ ID NO: 5.

Figure 6 is the amino acid sequence of BVH-28 protein; SEQ 30 ID NO: 6.

Figure 7 is the DNA sequence of BVH-3A gene which corresponds to the 5' terminal end of BVH-3; SEQ ID NO: 7.

Figure 8 is the amino acid sequence of BVH-3A protein; SEQ ID NO: 8.

Figure 9 is the DNA sequence of BVH-3B gene which

5 corresponds to the 3' terminal end of BVH-3; SEQ ID NO: 9.

Figure 10 is the amino acid sequence of BVH-3B protein; SEQ ID NO: 10.

Figure 11 depicts the comparison of the predicted amino acid sequences of the BVH-3 open reading frames from WU2, RX1, JNR.7/87, SP64, P4241 and A66 S. pneumoniae strains by using the program Clustal W from MacVector sequence analysis software (version 6.5). Underneath the alignment, there is a consensus line where * and . characters indicate identical and similar amino acid residues, respectively.

Figure 12 depicts the comparison of the predicted amino acid sequences of the BVH-11 open reading frames from WU2, Rx1, JNR.7/87, SP64, P4241, A66 and SP63 <u>S. pneumoniae</u> strains by using the program Clustal W from MacVector sequence analysis software (version 6.5). Underneath the alignment, there is a consensus line where * and . characters indicate identical and similar amino acid residues, respectively.

Figure 13 depicts the comparison of the predicted amino acid sequences of the BVH-11 proteins from various <u>S. pneumoniae</u> strains. The degrees of identity (I) and similarity (S) were determined by using the program Clustal W from MacVector sequence analysis software (version 6.5).

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Figure 14 is a DNA sequence containing the complete BVH-3 gene (open reading frame "ORF" at nucleotides 1777 to 4896); SEQ ID NO: 11.

Figure 15 is a DNA sequence containing the complete BVH-11 gene (ORF at nucleotides 45 to 2567); **SEQ ID NO: 12.**

5 Figure 16 is a DNA sequence containing the complete BVH-11-2 gene (ORF at nucleotides 114 to 2630); SEQ ID NO: 13.

Figure 17 is the amino acid sequence of BVH-11-2 protein; **SEQ ID NO: 14.**

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Figure 18 is the DNA sequence of SP63 BVH-3 gene; **SEQ ID** NO:15.

Figure 19 is the amino acid sequence of SP63 BVH-3 protein; 15 SEQ ID NO: 16.

Figure 20 is the amino acid sequence of BVH-3M protein; SEQ ID NO: 55.

20 Figure 21 is the amino acid sequence of BVH-3AD protein; SEQ ID NO: 56.

Figure 22 is the amino acid sequence of L-BVH-3-AD protein;

SEQ ID NO: 57.

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Figure 23 is the amino acid sequence of NEW12 protein; SEQ

ID NO: 58.

Figure 24 is the amino acid sequence of BVH-3C protein; SEQ 30 ID NO: 59.

Figure 25 is the amino acid sequence of BVH-11M protein; SEQ ID NO: 60.

35 Figure 26 is the amino acid sequence of BVH-11A protein; SEQ ID NO: 61.

Figure 27 is the amino acid sequence of BVH-11B (also called New13) protein; **SEQ ID NO: 62.**

5 Figure 28 is the amino acid sequence of BVH-11C protein; SEQ ID NO: 63.

Figure 29 is the amino acid sequence of NEW1 protein; SEQ ID NO: 64.

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Figure 30 is the amino acid sequence of NEW2 protein; **SEQ** ID NO: 65.

Figure 31 is the amino acid sequence of NEW3 protein; SEQ 15 ID NO: 66.

Figure 32 is the amino acid sequence of NEW4 protein; SEQ ID NO: 67.

20 Figure 33 is the amino acid sequence of NEW5 protein; SEQ ID NO: 68.

Figure 34 is the amino acid sequence of NEW6 protein; SEQ

ID NO: 69.

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Figure 35 is the amino acid sequence of NEW7 protein; **SEQ**ID NO: 70.

Figure 36 is the amino acid sequence of NEW8 protein; SEQ 30 ID NO: 71.

Figure 37 is the amino acid sequence of NEW9 protein; SEQ ID NO: 72.

Figure 38 is the amino acid sequence of BVH-11-2M protein; SEQ ID NO: 73.

Figure 39 is the amino acid sequence of NEW10 protein; SEQ ID NO: 74.

- 5 Figure 40 is the amino acid sequence of NEW11 protein; SEQ ID NO: 75.
 - Figure 41 is the DNA sequence of NEW12 gene; SEQ ID NO: 76.
- 10 Figure 42 is the amino acid sequence of NEW14 protein; SEQ ID NO: 77.

Figure 43 is the amino acid sequence of NEW15 protein; **SEQ** ID NO: 78.

Figure 44 is the amino acid sequence of NEW16 protein; SEQ ID NO: 79.

Figure 45 is the DNA sequence of GBS BVH-71 gene; **SEQ ID** 20 NO: 80.

Figure 46 is the amino acid sequence of GBS BVH-71 protein; SEQ ID NO: 81.

25 Figure 47 is the DNA sequence of GAS BVH-71 gene; **SEQ ID** NO:82.

Figure 48 is the amino acid sequence of GAS BVH-71 protein; SEQ ID NO:83.

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DETAILED DESCRIPTION OF THE INVENTION

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOS: 2, 4, 6, 8, 10, 14, 16, 55

to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 95% identity to a second polypeptide comprising a sequence chosen from **SEQ ID NOS: 2, 4, 6, 8, 10, 14, 16, 55** to **75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOS: 2, 4, 8, 10, 14, 16, 55 to

15 **75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from **SEQ ID NOs: 2, 4, 10, 14, 16, 55 to 75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 4, 8, 10, 14, 16, 55 to 75, 77 to 79 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 8, 10, 16, 55, 56, 57,

35 **58, 59, 64, 65, 66, 78** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 8, 10, 16, 55, 56, 57, 59, 64, 65, 66, 78 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at 10 least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 4, 14, 58, 60, 61, 62, 63, 67, 68, 69, 70, 71, 72, 73, 74, 75, 77, 79 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 4, 14, 60, 61, 62, 63, 67, 68, 69, 70, 71, 72, 73, 74, 75, 77, 79 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 4, 10, 14, 16, 55 to 75, 77 to 79 or fragments, analogs or derivatives thereof.

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30 According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence chosen from SEQ ID NOs: 10, 55 to 75, 77, 78, 79 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an

isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence chosen from **SEQ ID NOS:** 55 to 75, 77, 78, 79 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOs: 2, 4, 6, 8, 10 or

10 fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from SEQ ID NOS: 2, 4, 10, 14, 16 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence chosen from **SEQ ID NOS: 2, 4, 14, 16** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 2** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 4** or fragments, analogs or derivatives

35 thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 10** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 14** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 16** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence SEQ ID NO: 58 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence SEQ ID NO: 60 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 62** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 64** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO:** 67 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO:** 68 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence SEQ ID NO: 69 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence SEQ ID NO: 72 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at

least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 74** or fragments, analogs or derivatives

35 thereof.

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According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising sequence **SEQ ID NO: 77** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from **SEQ ID NOS: 2, 4, 6, 8, 10** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 8, 10, 14, 16, 55 to 75, 77 to 79 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 10, 14, 16, 55 to 75, 77 to 79 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from **SEQ ID NOs: 2, 4, 10, 14, 16** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 2 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence **SEQ ID NO: 4** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 10 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 14 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 16 or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from **SEQ ID NOs: 10, 55 to 75, 77, 78, 79** or fragments, analogs or derivatives thereof.

According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NO: 10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from SEQ ID NO: 10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from **SEQ ID NO: 10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence chosen from **SEQ ID NO: 10, 62, 64, 67, 68, 74, 77** or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 58 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 62 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 64 or fragments, analogs or derivatives thereof.

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According to one aspect, the present invention relates to

polypeptides characterized by the amino acid sequence comprising sequence **SEQ ID NO: 67** or fragments, analogs or derivatives thereof.

- According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 68 or fragments, analogs or derivatives thereof.
- 10 According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 74 or fragments, analogs or derivatives thereof.
- 15 According to one aspect, the present invention relates to polypeptides characterized by the amino acid sequence comprising sequence SEQ ID NO: 77 or fragments, analogs or derivatives thereof.
- 20 In a further embodiment, the present invention also relates to chimeric polypeptides which comprise one or more polypeptides or fragments, analogs or derivatives thereof as described in the present application.
- In a further embodiment, the present invention also relates to chimeric polypeptides which comprise one or more polypeptides or fragments, analogs or derivatives thereof as defined in the figures of the present application.

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- 30 In a further embodiment, the present application also relates to chimeric polypeptides which comprise two or more polypeptides chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof provided that the polypeptides or
- fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.

In a further embodiment, the chimeric polypeptide will comprise two or more polypeptides chosen from **SEQ ID**NOs:10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or

fragments, analogs or derivatives thereof; provided that the polypeptides or fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.

In a further embodiment, the chimeric polypeptide will comprise two or more polypeptides chosen from **SEQ ID**NOs:10, 58, 60, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof; provided that the polypeptides or fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.

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In a further embodiment, the chimeric polypeptide will comprise two or more polypeptides chosen from **SEQ ID**NOs:10, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof; provided that the polypeptides or fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.

In a further embodiment, the chimeric polypeptide will comprise between 2 and 5 polypeptides.

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In a further embodiment, the chimeric polypeptide will comprise between 2 and 4 polypeptides.

In a further embodiment, the chimeric polypeptide will comprise between 2 and 3 polypeptides.

In a further embodiment, the chimeric polypeptide will comprise 2 polypeptides.

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In a further embodiment, there is provided a chimeric polypeptide of formula (I): $\mathbf{A} - (\mathbf{B})_{n} - (\mathbf{C})_{n} - \mathbf{D} \quad (\mathbf{I})$

5 Wherein:

m is 0 or 1,

n is 0 or 1,

A is chosen from **SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83** or fragments, analogs or derivatives

10 thereof;

B is chosen from **SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof;

C is chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to

15 **75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof; and

D is chosen from **SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83** or fragments, analogs or derivatives thereof.

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In a further embodiment,

A is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or fragments, analogs or derivatives thereof;

- 25 B is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,
 69, 72, 74, 77, or fragments, analogs or derivatives
 thereof;
 - C is chosen from **SEQ ID NOs** :10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or fragments, analogs or derivatives
- 30 thereof; and
 D is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,
 69, 72, 74, 77 or fragments, analogs or derivatives
 thereof.
- 35 In a further embodiment,

A is chosen from SEQ ID NOS:10, 58, 60, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof; B is chosen from SEQ ID NOS:10, 58, 60, 62, 64, 67, 68, 74, 77, or fragments, analogs or derivatives thereof; C is chosen from SEQ ID NOS:10, 58, 60, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof; and D is chosen from SEQ ID NOS:10, 58, 60, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof.

- In one embodiment, chimeric polypeptides of the present invention comprise those wherein the following embodiments are present, either independently or in combination.
- In a further embodiment, A is SEQ ID NOs:10, 58, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof.

In a further embodiment, A is SEQ ID NO :10 or fragments, analogs or derivatives thereof.

- In a further embodiment, A is SEQ ID NO :58 or fragments,
- 20 analogs or derivatives thereof.

 In a further embodiment, A is SEQ ID NO :62 or fragments,

 analogs or derivatives thereof.

 In a further embodiment, A is SEQ ID NO :64 or fragments,
 - 25 In a further embodiment, A is SEQ ID NO :67 or fragments, analogs or derivatives thereof.

analogs or derivatives thereof.

- In a further embodiment, A is SEQ ID NO :68 or fragments, analogs or derivatives thereof.
- In a further embodiment, A is SEQ ID NO :74 or fragments,
- 30 analogs or derivatives thereof.
 In a further embodiment, A is SEQ ID NO :77 or fragments, analogs or derivatives thereof.

In a further embodiment, B is SEQ ID NOs:10, 58, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof.

In a further embodiment, B is SEQ ID NO :10 or fragments,

5 analogs or derivatives thereof.

In a further embodiment, **B** is **SEQ ID NO :58** or fragments, analogs or derivatives thereof.

In a further embodiment, **B** is **SEQ ID NO :64** or fragments, analogs or derivatives thereof.

In a further embodiment, B is SEQ ID NO :64 or fragments, analogs or derivatives thereof.

In a further embodiment, **B** is **SEQ ID NO :67** or fragments, analogs or derivatives thereof.

In a further embodiment, B is SEQ ID NO :68 or fragments,

15 analogs or derivatives thereof.

In a further embodiment, **B** is **SEQ ID NO :74** or fragments, analogs or derivatives thereof.

In a further embodiment, **B** is **SEQ ID NO : 77** or fragments, analogs or derivatives thereof.

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In a further embodiment, C is SEQ ID NOs:10, 58, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO :10 or fragments,

25 analogs or derivatives thereof.

In a further embodiment, **C** is **SEQ ID NO :58** or fragments, analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO: 62 or fragments, analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO :64 or fragments, analogs or derivatives thereof.

In a further embodiment, **C** is **SEQ ID NO: 67** or fragments, analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO: 68 or fragments,

analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO: 74 or fragments, analogs or derivatives thereof.

In a further embodiment, C is SEQ ID NO: 77 or fragments,

5 analogs or derivatives thereof.

In a further embodiment, D is SEQ ID NO:10, 58, 62, 64, 67, 68, 74, 77 or fragments, analogs or derivatives thereof.

- 10 In a further embodiment, D is SEQ ID NO :10 or fragments, analogs or derivatives thereof.
 - In a further embodiment, **D** is **SEQ ID NO :58** or fragments, analogs or derivatives thereof.

In a further embodiment, D is SEQ ID NO :62 or fragments,

- 15 analogs or derivatives thereof.
 - In a further embodiment, \mathbf{D} is **SEQ ID NO :64** or fragments, analogs or derivatives thereof.
 - In a further embodiment, **D** is **SEQ ID NO :67** or fragments, analogs or derivatives thereof.
- 20 In a further embodiment, D is SEQ ID NO :68 or fragments, analogs or derivatives thereof.
 - In a further embodiment, **D** is **SEQ ID NO :74** or fragments, analogs or derivatives thereof.
- In a further embodiment, D is SEQ ID NO :77 or fragments,
 - 25 analogs or derivatives thereof.

In a further embodiment, m is 0.

In a further embodiment, n is 0.

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In a further embodiment, m and n are 0.

In a further embodiment, **m** and **n** are 0, **A** is **SEQ ID NO:64** or fragments, analogs or derivatives thereof, **B** is **SEQ ID**

NO:62 or fragments, analogs or derivatives thereof.

In a further embodiment, **m** and **n** are 0, **A** is **SEQ ID NO:62**or fragments, analogs or derivatives thereof, **B** is **SEQ ID**NO:64 or fragments, analogs or derivatives thereof.

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In accordance with the present invention, all nucleotides encoding polypeptides and chimeric polypeptides are within the scope of the present invention.

10 In a further embodiment, the polypeptides or chimeric polypeptides in accordance with the present invention are antigenic.

In a further embodiment, the polypeptides or chimeric polypeptides in accordance with the present invention can elicit an immune response in an individual.

In a further embodiment, the present invention also relates to polypeptides which are able to raise antibodies having binding specificity to the polypeptides or chimeric polypeptides of the present invention as defined above.

An antibody that " has binding specificity" is an antibody that recognizes and binds the selected polypeptide but which does not substantially recognize and bind other molecules in a sample, e.g., a biological sample, which naturally includes the selected peptide. Specific binding can be measured using an ELISA assay in which the selected polypeptide is used as an antigen.

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Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In

case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

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As used herein, "fragments", "derivatives" or "analogs" of the polypeptides of the invention include those polypeptides in which one or more of the amino acid residues are substituted with a conserved or non-conserved 10 amino acid residue (preferably conserved) and which may be natural or unnatural. In one embodiment, derivatives and analogs of polypeptides of the invention will have about 70% identity with those sequences illustrated in the figures or fragments thereof. That is, 70% of the residues are the same. In a further embodiment, polypeptides will 15 have greater than 75% homology. In a further embodiment, polypeptides will have greater than 80% homology. In a further embodiment, polypeptides will have greater than 85% homology. In a further embodiment, polypeptides will have 20 greater than 90% homology. In a further embodiment, polypeptides will have greater than 95% homology. In a further embodiment, polypeptides will have greater than 99% homology. In a further embodiment, derivatives and analogs of polypeptides of the invention will have fewer than about 20 amino acid residue substitutions, modifications or 25 deletions and more preferably less than 10. Preferred substitutions are those known in the art as conserved i.e. the substituted residues share physical or chemical properties such as hydrophobicity, size, charge or 30 functional groups.

In accordance with the present invention, polypeptides of the invention include both polypeptides and chimeric polypeptides.

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Also included are polypeptides which have fused thereto

other compounds which alter the polypeptides biological or pharmacological properties i.e. polyethylene glycol (PEG) to increase half-life; leader or secretory amino acid sequences for ease of purification; prepro- and pro-sequences; and (poly)saccharides.

Furthermore, in those situations where amino acid regions are found to be polymorphic, it may be desirable to vary one or more particular amino acids to more effectively mimic the different epitopes of the different streptococcus strains.

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Moreover, the polypeptides of the present invention can be modified by terminal -NH₂ acylation (eg. by acetylation, or thioglycolic acid amidation, terminal carbosy amidation, e.g. with ammonia or methylamine) to provide stability, increased hydrophobicity for linking or binding to a support or other molecule.

- 20 Also contemplated are hetero and homo polypeptide multimers of the polypeptide fragments, analogues and derivatives.

 These polymeric forms include, for example, one or more polypeptides that have been cross-linked with cross-linkers such as avidin/biotin, gluteraldehyde or dimethyl-
- superimidate. Such polymeric forms also include polypeptides containing two or more tandem or inverted contiguous sequences, produced from multicistronic mRNAs generated by recombinant DNA technology.

 Preferably, a fragment, analog or derivative of a
- 30 polypeptide of the invention will comprise at least one antigenic region i.e. at least one epitope.

In order to achieve the formation of antigenic polymers (i.e. synthetic multimers), polypeptides may be utilized having bishaloacetyl groups, nitroarylhalides, or the like, where the reagents being specific for thio groups.

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Therefore, the link between two mercapto groups of the different peptides may be a single bond or may be composed of a linking group of at least two, typically at least four, and not more than 16, but usually not more than about 14 carbon atoms.

In a particular embodiment, polypeptide fragments, analogs and derivatives of the invention do not contain a methionine (Met) starting residue. Preferably,

10 polypeptides will not incorporate a leader or secretory sequence (signal sequence). The signal portion of a polypeptide of the invention may be determined according to established molecular biological techniques. In general, the polypeptide of interest may be isolated from a

15 streptococcus culture and subsequently sequenced to determine the initial residue of the mature protein and therefore the sequence of the mature polypeptide.

According to another aspect, there are provided vaccine 20 compositions comprising one or more streptococcus polypeptides of the invention in admixture with a pharmaceutically acceptable carrier diluent or adjuvant. Suitable adjuvants include oils i.e. Freund's complete or incomplete adjuvant; salts i.e. AlK(SO,), AlNa(SO,), -25 AlNH, (SO,), silica, kaolin, carbon polynucleotides i.e. poly IC and poly AU. Preferred adjuvants include QuilA and Alhydrogel. Vaccines of the invention may be administered parenterally by injection, rapid infusion, nasopharyngeal absorption, dermoabsorption, or bucal or oral. 30 Pharmaceutically acceptable carriers also include tetanus toxoid.

Vaccine compositions of the invention are used for the treatment or prophylaxis of streptococcus infection and/or diseases and symptoms mediated by streptococcus infection as described in P.R. Murray (Ed, in chief), E.J. Baron, M.A.

Pfaller, F.C. Tenover and R.H. Yolken. Manual of Clinical Microbiology, ASM Press, Washington, D.C. sixth edition, 1995, 1482p which are herein incorporated by reference. In one embodiment, vaccine compositions of the present

- invention are used for the treatment or prophylaxis of meningitis, otitis media, bacteremia or pneumonia. In one embodiment, vaccine compositions of the invention are used for the treatment or prophylaxis of streptococcus infection and/or diseases and symptoms mediated by streptococcus
- infection, in particular <u>S.pneumoniae</u>, group A streptococcus (pyogenes), group B streptococcus (GBS or agalactiae), dysgalactiae, uberis, nocardia as well as Staphylococcus aureus. In a further embodiment, the streptococcus infection is <u>S.pneumoniae</u>.

In a particular embodiment, vaccines are administered to those individuals at risk of streptococcus infection such as infants, elderly and immunocompromised individuals.

20 As used in the present application, the term "individuals" include mammals. In a further embodiment, the mammal is human.

Vaccine compositions are preferably in unit dosage form of

25 about 0.001 to 100 μg/kg (antigen/body weight) and more

preferably 0.01 to 10 μg/kg and most preferably 0.1 to 1

μg/kg 1 to 3 times with an interval of about 1 to 6 week

intervals between immunizations.

According to another aspect, there are provided polynucleotides encoding polypeptides characterized by the amino acid sequence chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

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In one embodiment, polynucleotides are those illustrated in SEQ ID Nos: 1, 3, 5, 7, 9, 11, 12, 13, 15, 76, 80, 82 which may include the open reading frames (ORF), encoding polypeptides of the invention. It will be appreciated that the polynucleotide sequences illustrated in the figures may be altered with degenerate codons yet still encode the polypeptides of the invention. Accordingly the present invention further provides polynucleotides which hybridize to the polynucleotide sequences herein above described (or 10 the complement sequences thereof) having 50% identity between sequences. In one embodiment, at least 70% identity between sequences. In one embodiment, at least 75% identity between sequences. In one embodiment, at least 80% identity between sequences. In one embodiment, at least 85% identity between sequences. In one embodiment, at least 90% identity 15 between sequences. In a further embodiment, polynucleotides are hybridizable under stringent conditions i.e. having at least 95% identity. In a further embodiment, more than 97% identity.

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In a further embodiment, polynucleotides are those illustrated in **SEQ ID NOs**: 1, 3, 7, 9, 11, 12, 13, 15, 76, 80, 82 encoding polypeptides of the invention.

- In a further embodiment, polynucleotides are those illustrated in SEQ ID NOs: 1, 3, 9, 11, 12, 13, 15, 76, 80, 82 which may include the open reading frames (ORF), encoding polypeptides of the invention.
- In a further embodiment, polynucleotides are those illustrated in **SEQ ID NOS**: 1, 3, 9, 11, 12, 13, 15, 76 which may include the open reading frames (ORF), encoding polypeptides of the invention.
- 35 In a further embodiment, polynucleotides are those

illustrated in **SEQ ID NOs**: 1, 3, 7, 9, 11, 12, 13, 15, 76 which may include the open reading frames (ORF), encoding polypeptides of the invention.

- 5 In a further embodiment, polynucleotides are those illustrated in **SEQ ID NOs**: 1, 7, 9, 11, 15, 76 which may include the open reading frames (ORF), encoding polypeptides of the invention.
- In a further embodiment, polynucleotides are those illustrated in SEQ ID NOS: 1, 9, 11, 15, 76 which may include the open reading frames (ORF), encoding polypeptides of the invention.
- In a further embodiment, polynucleotides are those illustrated in **SEQ ID NOS**: 1, 7, 9, 11 which may include the open reading frames (ORF), encoding polypeptides of the invention.
- In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO: 1**, encoding polypeptides of the invention.

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In a further embodiment, polynucleotides are those

25 illustrated in **SEQ ID NO :7,** encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :9,** encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :11**, encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :15**, encoding polypeptides of the invention.

5 In a further embodiment, polynucleotides are those illustrated in **SEQ ID NOs**: 3, 12, 13, 76, encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :3,** encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :12**, encoding polypeptides of the invention.

In a further embodiment, polynucleotides are those illustrated in **SEQ ID NO :13**, encoding polypeptides of the invention.

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In a further embodiment, polynucleotides are those illustrated in SEQ ID NO:76, encoding polypeptides of the invention.

25 As will be readily appreciated by one skilled in the art, polynucleotides include both DNA and RNA.

The present invention also includes polynucleotides complementary to the polynucleotides described in the present application.

In a further aspect, polynucleotides encoding polypeptides of the invention, or fragments, analogs or derivatives thereof, may be used in a DNA immunization method. That

35 is, they can be incorporated into a vector which is

replicable and expressible upon injection thereby producing the antigenic polypeptide in vivo. For example polynucleotides may be incorporated into a plasmid vector under the control of the CMV promoter which is functional in eukaryotic cells. Preferably the vector is injected intramuscularly.

According to another aspect, there is provided a process for producing polypeptides of the invention by recombinant techniques by expressing a polynucleotide encoding said polypeptide in a host cell and recovering the expressed polypeptide product. Alternatively, the polypeptides can be produced according to established synthetic chemical techniques i.e. solution phase or solid phase synthesis of oligopeptides which are ligated to produce the full polypeptide (block ligation).

polynucleotides and polypeptides are described in the 20 following references: Sambrook et al, Molecular Cloning: A Laboratory Manual, 2nd ed, Cold Spring Harbor, N.Y., 1989; Current Protocols in Molecular Biology, Edited by Ausubel F.M. et al., John Wiley and Sons, Inc. New York; PCR Cloning Protocols, from Molecular Cloning to Genetic 25 Engineering, Edited by White B.A., Humana Press, Totowa, New Jersey, 1997, 490 pages; Protein Purification, Principles and Practices, Scopes R.K., Springer-Verlag, New York, 3rd Edition, 1993, 380 pages; Current Protocols in Immunology, Edited by Coligan J.E. et al., John Wiley & Sons Inc., New York which are herein incorporated by 30 reference.

General methods for obtention and evaluation of

For recombinant production, host cells are transfected with vectors which encode the polypeptide, and then cultured in a nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes.

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Suitable vectors are those that are viable and replicable in the chosen host and include chromosomal, non-chromosomal and synthetic DNA sequences e.g. bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA. The polypeptide sequence may be incorporated in the vector at the appropriate site using restriction enzymes such that it is operably linked to an expression control region comprising a promoter, ribosome binding site (consensus region or Shine-Dalgarno sequence), and optionally an operator 10 (control element). One can select individual components of the expression control region that are appropriate for a given host and vector according to established molecular biology principles (Sambrook et al, Molecular Cloning: A Laboratory Manual, 2nd ed, Cold Spring Harbor, N.Y., 1989; Current Protocols in Molecular Biology, Edited by Ausubel F.M. et al., John Wiley and Sons, Inc. New York incorporated herein by reference). Suitable promoters include but are not limited to LTR or SV40 promoter, E.coli lac, tac or trp promoters and the phage lambda P, promoter. 20 Vectors will preferably incorporate an origin of replication as well as selection markers i.e. ampicilin resistance gene. Suitable bacterial vectors include pET, pQE70, pQE60, pQE-9, pbs, pD10 phagescript, psiX174, pbluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A, 25 ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 and eukaryotic vectors pBlueBacIII, pWLNEO, pSV2CAT, pOG44, pXT1, pSG, pSVK3, pBPV, pMSG and pSVL. Host cells may be bacterial i.e. E.coli, Bacillus subtilis, Streptomyces; fungal i.e. Aspergillus niger, Aspergillus nidulins; yeast i.e. 30 Saccharomyces or eukaryotic i.e. CHO, COS.

Upon expression of the polypeptide in culture, cells are typically harvested by centrifugation then disrupted by physical or chemical means (if the expressed polypeptide is not secreted into the media) and the resulting crude

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extract retained to isolate the polypeptide of interest. Purification of the polypeptide from culture media or lysate may be achieved by established techniques depending on the properties of the polypeptide i.e. using ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxylapatite chromatography and lectin chromatography. Final purification may be achieved using HPLC.

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The polypeptide may be expressed with or without a leader or secretion sequence. In the former case the leader may be removed using post-translational processing (see US 4,431,739; US 4,425,437; and US 4,338,397 incorporated herein by reference) or be chemically removed subsequent to purifying the expressed polypeptide.

According to a further aspect, the streptococcus polypeptides of the invention may be used in a diagnostic test for streptococcus infection, in particular <u>S. pneumoniae</u> infection. Several diagnostic methods are possible, for example detecting streptococcus organism in a biological sample, the following procedure may be followed:

- a) obtaining a biological sample from a patient;
- 25 b) incubating an antibody or fragment thereof reactive with a streptococcus polypeptide of the invention with the biological sample to form a mixture; and
 - c) detecting specifically bound antibody or bound fragment in the mixture which indicates the presence of streptococcus.

Alternatively, a method for the detection of antibody specific to a streptococcus antigen in a biological sample containing or suspected of containing said antibody may be performed as follows:

a) obtaining a biological sample from a patient;

b) incubating one or more streptococcus polypeptides of the invention or fragments thereof with the biological sample to form a mixture; and

c) detecting specifically bound antigen or bound fragment in the mixture which indicates the presence of antibody specific to streptococcus.

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- One of skill in the art will recognize that this diagnostic test may take several forms, including an immunological test such as an enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay or a latex agglutination assay, essentially to determine whether antibodies specific for the protein are present in an organism.
- The DNA sequences encoding polypeptides of the invention may also be used to design DNA probes for use in detecting the presence of streptococcus in a biological sample suspected of containing such bacteria. The detection method of this invention comprises:
- 20 a) obtaining the biological sample from a patient;
 - b) incubating one or more DNA probes having a DNA sequence encoding a polypeptide of the invention or fragments thereof with the biological sample to form a mixture; and
- 25 c) detecting specifically bound DNA probe in the mixture which indicates the presence of streptococcus bacteria.

The DNA probes of this invention may also be used for

detecting circulating streptococcus i.e.

S.pneumoniaenucleic acids in a sample, for example using a
polymerase chain reaction, as a method of diagnosing
streptococcus infections. The probe may be synthesized
using conventional techniques and may be immobilized on a

solid phase, or may be labelled with a detectable label. A
preferred DNA probe for this application is an oligomer

having a sequence complementary to at least about 6 contiguous nucleotides of the streptococcus pneumoniae polypeptides of the invention.

- 5 Another diagnostic method for the detection of streptococcus in a patient comprises:
 - a) labelling an antibody reactive with a polypeptide of the invention or fragment thereof with a detectable label;
- 10 b) administering the labelled antibody or labelled fragment to the patient; and
 - c) detecting specifically bound labelled antibody or labelled fragment in the patient which indicates the presence of streptococcus.

15

- A further aspect of the invention is the use of the streptococcus polypeptides of the invention as immunogens for the production of specific antibodies for the diagnosis and in particular the treatment of streptococcus infection.
- Suitable antibodies may be determined using appropriate screening methods, for example by measuring the ability of a particular antibody to passively protect against streptococcus infection in a test model. One example of an animal model is the mouse model described in the examples
- 25 herein. The antibody may be a whole antibody or an antigen-binding fragment thereof and may belong to any immunoglobulin class. The antibody or fragment may be of animal origin, specifically of mammalian origin and more specifically of murine, rat or human origin. It may be a
- 30 natural antibody or a fragment thereof, or if desired, a recombinant antibody or antibody fragment. The term recombinant antibody or antibody fragment means antibody or antibody fragment which was produced using molecular biology techniques. The antibody or antibody fragments may
- 35 be polyclonal, or preferably monoclonal. It may be specific for a number of epitopes associated with the

streptococcus pneumoniae polypeptides but is preferably specific for one.

Without limiting its scope, the present invention also
relates to new antigens designated BVH-3, BVH-11, BVH-11-2,
BVH-28 and BVH-71. The present invention also relates to
truncated polypeptides comprising fragments of the new
antigens designated BVH-3, BVH-11, BVH-11-2, BVH-28 and
BVH-71. The present invention also relates to chimeric
polypeptides comprising fragments of the new antigens
designated BVH-3, BVH-11, BVH-11-2, BVH-28 and BVH-71. The
following is a reference table summarizing the relation
between the antigens of the present invention:

Family	Nucleotide SEQ ID	Polypeptide SEQ ID
BVH-3		
BVH-3	1, 11	2
BVH-3A	7	8
BVH-3B	9	10
BVH-3 SP63	15	16
BVH-3M		55
BVH-3AD		56
L-BVH-3AD		57
New12	76	58
BVH-3C		59
Newl	·	64
New2		65
New3		66
New15		78
BVH-11		•
BVH-11	3, 12	4
BVH-11-2	13	14
BVH-11M		60
BVH-11A		61
BVH-11B also		62
referred to as		
NEW13		
BVH-11C		63
New4		67
New5		68

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Family	Nucleotide SEQ ID	Polypeptide SEQ ID NO
New6		69
New7		70
New8		71
New9		72
BVH-11-2M		73
New10		74
New11		75
New12	76	58
New14		77
New16		79
BVH-28		
BVH-28	5	6
BVH-71		
GBS	80	81
GAS	82	83

EXAMPLE 1

5 This example illustrates the cloning of S. pneumoniae genes.

The coding region of <u>S. pneumoniae</u> gene BVH-3 (**SEQ ID NO: 1**) and the coding region of <u>S. pneumoniae</u> gene BVH-28 (**SEQ ID NO: 5**) were amplified by PCR (DNA Thermal Cycler GeneAmp 10 PCR system 2400 Perkin Elmer, San Jose, CA) from genomic DNA of serogroup 6 <u>S. pneumoniae</u> strain SP64 using the oligos that contained base extensions for the addition of restriction sites BglII (AGATCT) and XbaI (TCTAGA). PCR products were purified from agarose gel using a QIAquick gel extraction kit from QIAgen (Chatsworth, CA), digested BglII-XbaI (Pharmacia Canada Inc, Baie d'Urfé, Canada), extracted with phenol: chloroform and precipitated with ethanol. The Superlinker vector pSL301 (Invitrogen, San Diego, CA) was digested with BglII and XbaI and purified from agarose gel using a QIAquick gel extraction kit from QIAgen (Chatsworth, CA). The BglII-XbaI genomic DNA fragments were ligated to

the BglII-XbaI pSL301 vector. The ligated products were transformed into E. coli strain DH5a [f80 lacZ DM15 endA1 recAl hsdR17 ("K-"K+) supE44 thi-11 gyrA96 relAl D(lacZYAargF)U169] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed), pp. 109-135). Recombinant pSL301 plasmids (rpSL301) containing either BVH-3 or BVH-28 gene were purified using a QIAgen kit (Chatsworth, CA) and DNA inserts were confirmed by nucleotide sequence analysis (Taq Dye Deoxy Terminator Cycle Sequencing kit, ABI, Foster City, 10 CA). Recombinant rpSL301 (rpSL301) were digested with the restriction enzymes BglII (AGATCT) and XhoI (CTCGAG). DNA fragments BglII-XhoI were purified using the QIAquick gel extraction kit from QIAgen (Chatsworth, CA). pET-32c(+) expression vector (Novagen, Madison, WI) containing the thioredoxin-His Tag sequence was digested with BamHI (GGATCC) and XhoI and gel extracted using the QIAquick gel extraction kit from QIAgen (Chatsworth, CA). The BglII-XhoI DNA fragments were ligated to the BamHI-XhoI pET-32c(+) vector to create the coding sequence for thioredoxin-20 His Tag-BVH-3 or thioredoxin-His Tag-BVH-28 fusion protein. The ligated products were transformed into E. coli strain DH5a [f80 lac2 DM15 endA1 recA1 hsdR17 ("K-"K+) supE44 thi-11 gyrA96 relA1 D(lacZYA-argF)U169] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA 25 Cloning, 1985, D.M. Glover (ed), pp. 109-135). Recombinant pET-32c(+) plasmids were purified using a QIAgen kit (Chatsworth, CA) and the nucleotide sequences at the fusion sites of thioredoxin-His Tag and DNA insert were verified by DNA sequencing (Taq Dye Deoxy Terminator Cycle Sequencing 30 kit, ABI, Foster City, CA).

EXAMPLE 2

This example illustrates the cloning of <u>S. pneumoniae</u> protein genes in CMV plasmid pCMV-GH.

The DNA coding region of a <u>S. pneumoniae</u> protein was inserted in phase downstream of a human growth hormone (hGH) gene which was under the transcriptional control of the cytomegalavirus (CMV) promotor in the plasmid vector pCMV-GH (Tang et al., Nature, 1992, 356:152). The CMV promotor is non functional plasmid in <u>E. coli</u> cells but active upon administration of the plasmid in eukaryotic cells. The vector also incorporated the ampicillin resistance gene.

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The coding region of BVH-3 gene (SEQ ID NO: 1) and BVH-28 gene (SEQ ID NO: 5) were obtained from rpSL301 (see example 1) using restriction enzymes BglII (AGATCT) and XbaI (TCTAGA). The digested products were purified from agarose 20 gel using the QIAquick gel extraction kit from QIAgen (Chatsworth, CA). The pCMV-GH vector (Laboratory of Dr. Stephen A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas) containing the human growth hormone to create fusion proteins was digested with BglII and XbaI and purified from agarose gel using the 25 QIAquick gel extraction kit from QIAgen (Chatsworth, CA). The BglII-XbaI DNA fragments were ligated to the BglII-XbaI pCMV-GH vector to create the hGH-BVH-3 or hGH-BVH-28 fusion protein under the control of the CMV promoter. The ligated products were transformed into E. coli strain DH5a[f80 lacZ 30 DM15 endA1 recA1 hsdR17 ("K-"K+") supE44 thi-11 gyrA96 relA1 D(lacZYA-argF)U169] (Gibco BRL, Gaithersburg, MD) according

to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed), pp. 109-135). The recombinant pCMV plasmids were purified using a QIAgen kit (QIAgen, Chatsworth, CA).

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The coding region of BVH-11 gene (SEQ ID NO: 3) was amplified by PCR (DNA Thermal Cycler GeneAmp PCR system 2400 Perkin Elmer, San Jose, CA) from genomic DNA of serogroup 6 S. pneumoniae strain SP64 using the oligos that contained 10 base extensions for the addition of restriction sites BglII (AGATCT) and HindIII (AAGCTT). The PCR product was purified from agarose gel using a QIAquick gel extraction kit from QIAgen (Chatsworth, CA), digested with restriction enzymes (Pharmacia Canada Inc, Baie d'Urfe, Canada), extracted with phenol: chloroform and precipitated with ethanol. 15 pCMV-GH vector (Laboratory of Dr. Stephen A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas) was digested with BglII and HindIII and purified from agarose gel using the QIAquick gel extraction kit from QIAgen (Chatsworth, CA). The BglII-HindIII DNA fragment was 20 ligated to the BglII-HindIII pCMV-GH vector to create the hGH-BVH-11 fusion protein under the control of the CMV promoter. The ligated products were transformed into E. coli strain DH5a[f80 lacZ DM15 endAl recAl hsdR17 (*K-mK*) supE44 thi-11 gyrA96 relA1 D(lacZYA-argF)U169] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed), pp. 109-135). The recombinant pCMV plasmid was purified using a QIAgen kit (Chatsworth, CA) and the nucleotide sequence of 30 the DNA insert was verified by DNA sequencing.

EXAMPLE 3

This example illustrates the use of DNA to elicit an immune response to S. pneumoniae antigens.

5

A group of 8 female BALB/c mice (Charles River, St-Constant, Québec, Canada) were immunized by intramuscular injection of 50 μl three times at two- or three-week intervals with 100 μg of recombinant pCMV-GH encoding the BVH-3, BVH-11 or the 10 BVH-28 gene in presence of 50 µg of granulocyte-macrophage colony-stimulating factor (GM-CSF) - expressing plasmid pCMV-GH-GM-CSF (Laboratory of Dr. Stephen A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas). As control, a group of mice were injected with 100 µg of 15 pCMV-GH in presence of 50 µg of pCMV-GH-GM-CSF. Blood samples were collected from the orbital prior to each immunization and seven days following the third injection and serum antibody responses were determined by ELISA using thioredoxin-His Tag-S. pneumoniae fusion protein as coating 20 antigen. DNA immunization with recombinant plasmid pCMV-GH encoding the BVH-3, BVH-11 or the BVH-28 S. pneumoniae protein induced antibody reactive against the respective recombinant protein. The reciprocal antibody titers, defined as the highest serum dilution at which the absorbance values 25 were 0.1 above the background values, were above 4x103.

EXAMPLE 4

30 This example illustrates the production and purification of recombinant <u>S. pneumoniae</u> proteins.

The recombinant pET plasmids containing the BVH-3, BVH-11 or the BVH-28 gene corresponding to the SEQ ID NO: 1 , SEQ ID NO: 3 or the SEQ ID NO: 5 respectively were transformed by electroporation (Gene Pulser II apparatus, BIO-RAD Labs, Mississauga, Canada) into E. coli strain AD494 (DE3) (Dara leu7697 DlacX74 DphoA PvuII phoR DmalF3 F'[lac*(lacIq) pro] trxB::Kan) (Novagen, Madison, WI). In this strain of E. coli, the T7 promotor controlling expression of the fusion 10 protein is specifically recognized by the T7 RNA polymerase (present on the 1DE3 prophage) whose gene is under the control of the lac promotor which is inducible by isopropylß-d-thio-galactopyranoside (IPTG). The transformant AD494(DE3)/rpET was grown at 37°C with agitation at 250 rpm 15 in LB broth (peptone 10g/L, yeast extract 5g/L, NaCl 10g/L) containing 100µg of ampicillin (Sigma-Aldrich Canada Ltd., Oakville, Canada) per ml until the A600 reached a value of 0.6. In order to induce the production of the thioredoxin-His Tag-BVH-3, thioredoxin-His Tag-BVH-11 or thioredoxin-20 His Tag-BVH-28 fusion protein, the cells were incubated for 2 additional hours in the presence of IPTG at a final concentration of 1 mM. Induced cells from a 100 ml culture were pelleted by centrifugation and frozen at -70°C.

25 The purification of the fusion proteins from the soluble cytoplasmic fraction of IPTG-induced AD494(DE3)/rpET was done by affinity chromatography based on the properties of the His·Tag sequence (6 consecutive histidine residues) to bind to divalent cations (Ni²⁺) immobilized on the His·Bind 30 metal chelation resin. Briefly, the pelleted cells obtained from a 100mL culture induced with IPTG were resuspended in

phosphate-buffered (PBS):500mM NaCl pH7.1, sonicated and spun at 20,000 X g for 20 min to remove debris. The supernatant was filtered (0.22µm pore size membrane) and deposited on a HiTrap® 1mL chelating pre-packed ready-to-use column (Pharmacia Biotech, Baie d'Urfé, Canada). The thioredoxin-His·Tag-S. pneumoniae fusion protein was eluted with 1M imidazole-500mM NaCl-PBS pH7.1. The removal of the salt and imidazole from the sample was done by dialysis against PBS at 4°C. The quantities of fusion protein obtained from the soluble fraction of E. coli was estimated by MicroBCA (Pierce, Rockford, Illinois).

EXAMPLE 5

15

This example illustrates the protection of mice against fatal pneumococcal infection by immunization.

Groups of 8 female BALB/c mice (Charles River) were

immunized subcutaneously three times at three-week intervals
with either 25 μg of affinity purified thioredoxin-His-TagBVH-3 fusion protein in presence of 15 μg of QuilA adjuvant
(Cedarlane Laboratories Ltd, Hornby, Canada) or, as control,
with QuilA adjuvant alone in PBS. Blood samples were

25 collected from the orbital sinus on day 1, 22 and 43 prior
to each immunization and seven days (day 50) following the
third injection. One week later the mice were challenged
with approximately 10⁶ CFU of the type 3 S. pneumoniae
strain WU2. Samples of the S. pneumoniae challenge inoculum
were plated on chocolate agar plates to determine the CFU
and to verify the challenge dose. Deaths were recorded for

a period of 14 days and on day 14 post-challenge, the surviving mice were sacrificied and blood samples tested for the presence of <u>S. pneumoniae</u> organisms. The survival data are shown in table 1.

5

10

Prechallenge sera were analyzed for the presence of antibodies reactive with <u>S. pneumoniae</u> by standard immunoassays. Elisa and immunoblot analyses indicated that immunization with recombinant <u>S. pneumoniae</u> protein produced in <u>E. coli</u> elicited antibodies reactive with both, recombinant and native pneumococcal protein.

Table 1. Protection mediated by recombinant BVH-3 protein

Immunogen	No. of mice alive : no. of mice	Median day of
	dead	death
	14 days post-challenge	
BVH-3	8 : 0	>14
none	0 : 8	1

15

20

All mice immunized with BVH-3 recombinant protein survived to infection while none of the control mice given adjuvant alone survived. There was a significant difference in survival between the two groups of mice (P<0.0001, log rank test for nonparametric analysis of survival curves; P=0.0002, Fisher's exact test). All hemocultures from surviving mice were negative at day 14 post-challenge.

25

EXAMPLE 6

This example describes the cloning of $\underline{BVH-3}$ and $\underline{BVH-11}$ genes from a variety of \underline{S} . pneumoniae strains and the molecular conservation of these genes.

- 5 Molecular analysis of chromosomal DNA from various <u>S. pneumoniae</u> isolates with DNA probes spanning different regions of <u>BVH-3</u> or <u>BVH-11</u> revealed the presence of one <u>BVH-3</u> gene copy and two <u>BVH-11</u> gene copies. The two <u>BVH-11</u> gene copies are not identical and the genes were arbitrarily designated <u>BVH-11</u> (SEQ ID NO:12; ORF at nucleotides 45 to 2567) and <u>BVH-11-2</u> (SEQ ID NO:13; ORF at nucleotides 114 to 2630).
- The first amino acids of the BVH-3 and BVH-11 coding

 regions have the characteristics of leader sequences also known as signal peptides. The consensus signal peptidase cleavage site L-X-X-C of lipoprotein modification/processing sites was present in the sequences. Mature BVH-3, BVH-11 and BVH-11-2 proteins from S.
- 20 pneumoniae SP64 have 1019, 821 and 819 amino acids, respectively. The regions of <u>S. pneumoniae</u> genes coding for mature BVH-3, termed BVH-3M, (nucleotides 1837 4896; SEQ. ID. NO: 11), BVH-11M (nucleotides 102-2567; SEQ. ID. NO: 12) and BVH-11-2M (nucleotides 171-2630; SEQ. ID. NO: 130 and BVH-11-2M (nucleotides 171-2630; SEQ. ID. NO: 140 and BVH-11-2M (nucleotides 171-2630; SEQ. ID. NO: 140 and BVH-11-2M (nucleotides 171-2630; SEQ. ID. NO: 140 and 140 amino acids, respectively.
- 25 13), were amplified by PCR(DNA Thermal Cycler GeneAmp PCR system 2400 Perkin Elmer, San Jose, CA) from genomic DNA of 6 or 7 <u>S. pneumoniae</u> strains. Serogroup 6 <u>S. pneumoniae</u> SP64 and serogroup 9 SP63 clinical isolates were provided by the laboratoire de la santé publique du Québec, Sainte-
- 30 Anne-de-Bellevue; serotype 4 strain JNR.7/87 was provided by Andrew Camilli, Tufts University School of Medicine, Boston; Rxl strain, a nonencapsulated derivative of the type 2 strain D39 and the type 3 strains A66 and WU2 were provided by David E. Briles from University of Alabama,
- 35 Birmingham and the type 3 clinical isolate P4241 was provided by the centre de recherche en infectiologie du

centre hospitalier de l'université Laval, Sainte-Foy. The sets of oligonucleotide primers OCRR479-OCRR480; HAMJ160-OCRR488 and HAMJ160-HAMJ186, that contained base extensions for the addition of restriction sites were used for the amplification of BVH-3, BVH-11 and BVH-11-2 gene, respectively, with the exception of BVH-11 gene from SP64 strain which was amplified using the set of primers consisting of HAMJ487 and OCRR488. Primer sequences are listed below (Table 2). PCR products were purified from agarose gel using a QIAquick gel extraction kit from QIAgen 10 (Chatsworth, CA) and digested BglII-XbaI or BglII-HindIII (Pharmacia Canada Inc, Baie d'Urfé, Canada). Digestions were cleaned using a QIAquick PCR purification kit from QIAgen (Chatsworth, CA). The PCR products were ligated to the BglII-XbaI or BglII-HindIII pSL301 vector. The ligated 15 products were transformed into <u>E. coli</u> strain DH5 α [ϕ 80 lacZ ΔM15 endA1 recA1 hsdR17 ('K'K') supE44 thi-1λ gyrA96 relA1 $\Delta(lacZYA-argF)U169$] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed), pp. 109-135). Recombinant 20 pSL301 plasmids (rpSL301) containing BVH-3, BVH-11 or BVH11-2 were purified using a QIAgen kit (Chatsworth, CA) and DNA inserts were sequenced (Taq Dye Deoxy Terminator Cycle Sequencing kit, ABI, Foster City, CA). The figures 11 and 12 depict the consensus sequence established from the . 25 BVH-3, and BVH-11 deduced amino acid sequences, respectively. Comparison of BVH-3 protein sequences revealed 99 to 100% identity of sequences for all strains with the exception that BVH-3 from serogroup 9 SP63 strain 30 (SEQ. ID. NO: 15 and SEQ. ID. NO: 16) misses a stretch of 177 amino acids corresponding to residues 244 to 420 on BVH-3' protein sequence of S. pneumoniae SP64. Analysis of sequences of additional serogroup 9 strains revealed BVH-3 molecule having the same deletion in 3 out of 4 strains

thus suggesting that the 3 strains are members of a \underline{S} . pneumoniae serogroup 9 clone.

Comparison of 13 BVH-11 nucleotide sequences obtained from 5 7 S. pneumoniae strains, revealed that the nucleotide sequences are very similar. Computer analysis (MacVector, Clustal W 1.4) using multiple alignment of the predicted BVH-11 protein sequences revealed that these sequences were 75% identical and 82% homologous on a length of 834 amino acids. Pairwise alignment revealed 80 to 100% identity 10 (Figure 13). The sequences showed great similarity in overall organization. Variability in the primary sequence of these proteins is almost restricted to the last 125 amino acids in the C-terminal portion of the proteins. This region constitutes a domain. Close examination of this domain revealed two groups of sequences. The first 9 sequences from the figure 13 belong to one group while the last 4 sequences belong to another group. A 39% identity value is obtained when the domain sequences of the 13 proteins are compared (MacVector, Clustal W 1.4). identity value increased to more than 92% when sequences belonging to a same group are compared.

25 EXAMPLE 7

This example illustrates the homology of portions of $\underline{BVH-3}$ and $\underline{BVH-11}$ genes.

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30 Molecular analysis with DNA probes derived from <u>BVH-3</u> and <u>BVH-11</u> genes indicated that <u>BVH-3</u> and <u>BVH-11</u> were related. In dot blot hybridization studies, DNA probe consisting of either, BVH-3 or BVH-11, gene sequence hybridized to both, <u>BVH-3</u> and <u>BVH-11</u> genes thus indicating that <u>BVH-3</u> and <u>BVH-3</u> and <u>BVH-11</u> genes shared homologous sequences. Comparison of sequences revealed that the ORFs and the proteins were 43

and 33% identical, respectively. Closer examination revealed that the region corresponding to amino acids 1 to 225 in BVH-3 and 1 to 228 in BVH-11 were 73 and 75% identical at the DNA and protein level, respectively. contrast, the 3' regions corresponding to amino acids 226 to 1039 from BVH-3 and amino acids 229-840 from BVH-11 were only 34 and 22% identical at the DNA and protein level, respectively. Thus the 5' termini of BVH-3 and BVH-11 genes appear to contain highly conserved sequences while 10 the remaining parts of the genes are highly divergent. These results suggest that BVH-3 and BVH-11 might share similar functions mediated by sequences present in the conserved region whereas BVH-3- and BVH-11-specific functions might be mediated by sequences in the divergent 15 region.

EXAMPLE 8

20 This example describes the cloning of truncated <u>BVH-3</u>, <u>BVH-11</u> and <u>BVH-11-2</u> genes by polymerase chain reaction (PCR) and the expression of truncated BVH-3 and BVH-11 molecules.

Gene fragments were amplified by PCR using pairs of 25 oligonucleotide engineered to amplify fragments spanning the BVH-3 (SEQ ID NO: 1 and SEQ ID NO: 11), BVH-11 (SEQ ID NO: 3 and SEQ ID NO: 12) or BVH-11-2 (SEQ ID NO: 13) gene from S. pneumoniae strain SP64. Each of the primers had a restriction endonuclease site at the 5' end, thereby 30 allowing directional in-frame cloning of the amplified product into the digested plasmid vector (Tables 2 and 3). PCR-amplified products were digested with restriction endonucleases and ligated to either linearized plasmid pSL301 (see example 1), pCMV-GH (see example 2) or pET (Novagen, Madison, WI) expression vector digested likewise 35 or digested with enzymes that produce compatible cohesive

ends. Recombinant pSL301 and recombinant pCMV-GH plasmids were digested with restriction enzymes for the in-frame cloning in pET expression vector. Clones were first stabilized in E. coli DH5\alpha before introduction into E. coli BL21(λDE3) or AD494 (λDE3) for expression of truncated BVH-3 or BVH-11 molecules. Each of the resultant plasmid constructs was confirmed by nucleotide sequence analysis. The recombinant proteins were expressed as N-terminal fusions with the thioredoxin and His-tag or as C-terminal 10 fusions with an His-tag. The expressed recombinant proteins were purified from supernatant fractions obtained from centrifugation of sonicated IPTG-induced E. coli cultures using a His-Bind metal chelation resin (OIAgen, Chatsworth, CA). The gene products generated are listed in 15 the table 3. The gene products corresponding to the Nterminal region including the signal sequence are designated as Lipidated-proteins or lipoproteins (Lproteins). The gene products corresponding to the Nterminal region lacking the signal sequence are identified 20 as protein without signal sequence (w/o ss).

Table 2. List of PCR oligonucleotide primers

Sequence 5' - 3'

25

Primer

SEQ.

OCRR 479 17 cagtagatetgtgcctatgcactaaac SEQ ID 1 :6178
OCRR 480 18 gatetetagactactgctattccttacgctatg SEQ
ID 11 :4909-

OCRR 497 19 atcactcgagcattacctggataatcctgt SEQ Though 1:15251506
OCRR 498 20 ctgctaagcttatgaaagatttagat SEQ HindIII
1:15341548

Restric-

tion sites

BglII

XbaI

Nucleotide

OCRR 499	21	gatactcgagctgctattccttac	SEQ ID 11 :4906- 4893	XhoI
HAMJ 172	22	gaatctcgagttaagctgctgctaattc	SEQ ID 1: 675-661	XhoI
НАМЈ 247	23	gacgctcgagcgctatgaaatcagataaattc	SEQ ID 1:3117-3096	Xhol
HAMJ 248	24	gacgctcgagggcattacctggataatcctgttcatg	SEQ ID 1:1527-1501	XhoI
НАМЈ 249	25	cagtagatetetteateatttattgaaaagagg	SEQ ID 11 : 1749-1771	BglII
HAMJ 278	26	ttatttcttccatatggacttgacagaagagcaaattaag	SEQ ID 1:1414-1437	Ndel
НАМЈ 279	27	cgccaagcttcgctatgaaatcagataaattc	SEQ ID 1:3117-3096	HindIII
HAMJ 280	28	cgccaagcttttccacaatataagtcgattgatt	SEQ ID 1:2400-2377	HindIII
HAMJ 281	29	ttatticticcatatggaagtacctatctiggaaaaagaa	SEQ ID 1:2398-2421	NdeI
НАМЈ 300	30	ttatticttccatatggtgcctatgcactaaaccagc	SEQ ID 1:62- 82	NdeI
HAMJ 313	31	ataagaatgeggeegetteeacaatataagtegattgatt	SEQ ID 1:2400-2377	NotI
OCRR 487	32	cagtagatctgtgcttatgaactaggtttgc	SEQ ID 3:58- 79	BgIII
OCRR 488	33	gatcaagettgetgetacetttacttactete	SEQ ID 12:2577-2556	HindIII
HAMJ 171	34	ctgagatatccgttatcgttcaaacc	SEQ ID 3:1060-1075	EcoRV
HAMJ 251	35	ctgcaagettttaaaggggaataatacg	SEQ ID 3:1059-1045	HindIII
HAMJ 264	36	cagtagatetgeagaageetteetatetg	SEQ ID 3 :682- 700	BglII
HAMJ 282	37	tegecaagettegttategtteaaaceattggg	SEQ ID 3:1060-1081	HindIII
НАМЈ 283	38	ataagaatgeggeegeettaeteteetttaataaageeaat agtt	3 :2520-2492	Ndel
HAMJ 284	39	catgccatggacattgatagtctcttgaaacagc	SEQ ID 3 :856- 880	Ncol
HAMJ 285	40	cgccaagcttcttactctcctttaataaagccaatag	SEQ ID 3:2520-2494	HindIII
HAMJ 286	41	cgacaagcttaacatggtcgctagcgttacc	SEQ ID 3:2139-2119	HindIII
HAMJ 287	42	cataccatgggcctttatgaggcacctaag	SEQ ID 3:2014-2034	Ncol
НАМЈ 288	43	cgacaagcttaagtaaatcttcagcctctctcag	SEQ ID 3:2376-2353	HindIII

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HAMJ 289	44	gataccatggctagcgaccatgttcaaagaa	SEQ ID 3 :2125-2146	Ncol
НАМЈ 290	45	cgccaagcttatcatccactaacttgactttatcac	SEQ ID 3:1533-1508	HindIII
HAMJ 291	46	cataccatggatattcttgccttcttagctccg	SEQ ID 3:1531-1554	NcoI
HAMJ 301	47	catgccatggtgcttatgaactaggtttgc	SEQ ID 3:59- 79	Ncol
HAMJ 302	48	cgccaagctttagcgttaccaaaaccattatc	SEQ ID 3:2128-2107	HindIII
HAMJ 160	49	gtattagatctgttcctatgaacttggtcgtcacca	SEQ ID 13: 172-196	BglII
HAMJ 186	50	cgcctctagactactgtataggagccgg	SEQ ID 13: 2460-2443	XbaI
HAMJ 292	51	catgccatggaaaacatttcaagccttttacgtg	SEQ ID 11: 754-778	Ncol
НАМЈ 293	52	cgacaagctictgtataggagccggttgactttc	SEQ ID 11: 2457-2434	HindIII
HAMJ 294	53	catgccatggttcgtaaaaataaggcagaccaag	SEQ ID 11: 2038-2062	Ncol
HAMJ 297	54	catgccatggaagcctattggaatgggaag	SEQ ID 11: 622-642	Ncol

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Lists of truncated BVH-3 and BVH-11 gene products generated from S. pneumoniae Table 3.

PCR-primer sets	Protein	Identification	SEQ.	Cloning
	designation	(encoded amino acids)	ID.NO.	vector
OCRR479-OCRR480	вун-3м	BVH-3 w/o ss (21-1039)	55	pSL301
OCRR479-OCRR497	вун-зар	BVH-3 N'end w/o ss (21-509)	56	pSL301
HAMJ248-HAMJ249	L-BVH-3AD	BVH-3 N'end (1-509)	57	pET-21(+)
OCRR498-OCRR499	вун-зв	BVH-3 C'end (512-1039)	10	pSL301
OCRR479-HAMJ172	BVH-3C	BVH-3 N' end w/o ss (21-225)	59	pET-32 c(+)
OCRR487-OCRR488	ВVН-11М	BVH-11 w/o ss (20-840)	09	pCMV-GH
HAMJ251-0CRR487	BVH-11A	BVH-11 N'end w/o ss (20-353)	61	pET-32 c (+)
HAMJ171-OCRR488	BVH-11B	BVH-11 C'end (354-840)	62	pET-32 a(+)
HAMJ264-OCRR488	BVH-11C	BVH-11 C'end (228-840)	63	pET-32 a(+)
HAMJ278-HAMJ279	NEW1	BVH-3 C'end (472-1039)	64	pET-21b(+)
HAMJ278-HAMJ280	NEW2	BVH-3 C'end (472-800)	. 29	pET-21b(+)
HAMJ281-HAMJ279	NEW3	BVH-3 C'end (800-1039)	99	pET-21b(+)
HAMJ284-HAMJ285	NEW4	BVH-11 C'end (286-840)	67	pET-21d(+)
HAMJ284-HAMJ286	NEWS	BVH-11 internal (286-713)	68	pET-21d(+)
HAMJ287-HAMJ288	NEW6	BVH-11 internal (672-792)	69	pET-21d(+)
HAMJ285-HAMJ289	NEW7	BVH-11 internal (709-840)	7.0	pET-21d(+)
HAMJ284-HAMJ290	NEW8	BVH-11 internal (286-511)	71	pET-21d(+)

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HAMJ286-HAMJ291	NEW9	BVH-11 internal (511-713)	72	pET-21d(+)
HAMJ160-HAMJ186	BVH-11-2M	BVH-11-2 w/o ss (20-838)	73	pSL301
HAMJ292-HAMJ293	NEW10	BVH-11-2 C'end (271-838)	74	pET-21d(+)
HAMJ293-HAMJ294	NEW11	BVH-11-2 C'end (699-838)	75	pET-21d(+)
HAMJ282-HAMJ283	BVH-11B	BVH-11 C'end (354-840)	62	pET-21b(+)
HAMJ286-HAMJ297	NEW14	BVH-11-2 internal (227-699)	77	pET-21d(+)
HAMJ300-HAMJ313	NEW15	BVH-3 N'end w/o ss (21-800)	78	pET-21b(+)
HAMJ301-HAMJ302	NEW16	BVH-11 N'end w/o ss (20-709)	79	pET-21d(+)

EXAMPLE 9

This example describes the isolation of monoclonal antibodies (Mabs) and the use of Mabs to characterize BVH-3, BVH-11 and BVH-11-2 protein epitopes.

Female BALB/c mice (Charles River) were immunized subcutaneously with BVH-3, BVH-11 or BVH-11-2 gene products from S. pneumoniae strain SP64 in presence of 15 μ g of 10 QuilA adjuvant (Cedarlane Laboratories Ltd, Hornby, Canada). One set of mice (fusion experiment 1) were immunized on day 1 and 14 with 25 μ g of affinity purified thioredoxin-His•Tag-BVH-3M fusion protein. A second group of mice (fusion experiment 2) were immunized three times at 15 three-week intervals with 25 μ g of affinity purified thioredoxin-His•Tag-BVH-11M. A third group of mice (fusion experiment 3) were immunized on day 1 and day 15 with 25 μq of affinity purified thioredoxin-HisoTag-BVH-11-2M fusion protein. A fourth group of mice (fusion experiment 4) were 20 immunized on day 1 with 25 μ g of affinity purified thioredoxin-His•BVH-11B fusion protein and boosted by intravenous injection on day 16 and on day 37 with recombinant BVH-11B in PBS. Three to four days before fusion, mice were injected intravenously with 25 μ g of the 25 respective antigen suspended in PBS alone. Hybridomas were produced by fusion of spleen cells with nonsecreting SP2/0 myeloma cells as previously described by J. Hamel et al. [J. Med. Microbiol., 23, pp163-170 (1987)]. Culture supernatants of hybridomas were initially screened by enzyme-linked-immunoassay according to the procedure . 30 described by Hamel et al. (Supra) using plates coated with preparations of purified recombinant proteins or suspensions of heat-killed S. pneumoniae cells. Positive hybridomas selected on the basis of ELISA reactivity with a

variety of antigens were then cloned by limiting dilutions, expanded and frozen.

Hybridomas were tested by ELISA or Western immunoblotting
against BVH-3 and BVH-11 gene products in order to
characterize the epitopes recognized by the Mabs. BVH-3
and BVH-11 shared common epitopes with 6 Mabs (H3-1-F9, H31-D4, H3-1-H12, H11-1-E7, H11-1-H10 and H11-1.1-G11)
showing reactivities with both proteins (Table 4). BVH-11
and BVH-11-2 molecules from S. pneumoniae SP64 shared
common epitopes not present on BVH-3 with Mabs (3A1, 13C11,
10H10, 1D8, 10G9, 10A2, 3E8, 10D7, 2H7 and 6H7) reactive
with both, BVH-11 and BVH-11-2, recombinant proteins (Table 5).

15

Table 4. Reactivity of BVH-3-immunoreactive Mabs with a panel of <u>BVH-3</u> and <u>BVH-11</u> gene products

	a.Immunoreactivity with							
MAbs	BVH-3M	BVH-3A	BVH-3B	BVH-3C	NEW2	NEW3	BVH-11M	
	21-1039	21-509	512-1039	21-225	472-800	800-1039	20-840	
H3-1-F9	+	+	_	+	-	-	+	
H3-1-D4	+	+	-	+		_	+	
H3-1-H12	+	+		+	-	-	+	
H3-2-G2	+	+	-	-	_	-		
H3-3-A1	+.	+	-	. -				
H3-4-D3	+	-	+	-	-	+	-	
H11-1-E7	+	+	_	+	_	_	+	
H11-1-	+	+	-	+	-	_	+	
н10								
H11-	+	+		+	+	_	+	
1.1-G11	1							

Table 5. Reactivity of Mabs raised against BVH-11-2 protein from <u>S. pneumoniae</u> strain SP64 with a panel of <u>BVH-11</u> gene products

	b.Immunoreactivity with						· · · · · · · · · · · · · · · · · · ·	
Mabs*				d.BVH-11-2 products				
	BVH-11M 20-840	NEW8 286-511	NEW9 511-713	BVH-11B 354-840	BVH-11-2 20-838	NEW10 271-838	NEW11 699-838	NEW14 227-699
3A1	+	+	-	+	+	+	-	+
13C1	+	+	+	+	+	+	-	+
10H10	+	+	+	+	+	+	-	+
1D8	+	+	-	+	+	+	-	+
10G9	+	_	-	+	+	+	-	+
10A2	+	-	-	+	+	+	-	+
3E8	+		-	+	+	+	-	+
10D7	+	-	_	+	+	+	_	+
2H7	+	-		_	+		_	-
6H7	+ .	_	-	-	+	-	-	_
3A4	-	-	_	-	+	+	+	-
14H6	1	-	_	-	+	+	+	-
7G2	•	-	_	_	+	+	-	+
13H10	-	-	-	-	+	-	-	+
7E8	1	_	-	_	+	-	_	_
7H6	_	-	1	_	+	-	-	-

^a Mabs listed in this table were not reactive with recombinant BVH-3 molecule

The results obtained from the immunoreactivity studies of the Mabs (Table 4 and Table 5) are in agreement with the protein sequences derived from the respective gene sequences. Indeed the Mabs cross-reactive with BVH-3 and BVH-11 molecules recognized BVH-3C protein corresponding to the conserved region, and BVH-11 and BVH-11-2 specific Mabs were reactive with epitopes located on variable parts of these molecules. BVH-3 and BVH-11, and BVH-11 and BVH-11-2 can be distinguished by their reactivity with Mabs.

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EXAMPLE 10

This example illustrates the simultaneous expression of BVH-3 and BVH-11 gene products by S. pneumoniae.

A standard Western blot technique was used to investigate 5 whether <u>BVH-3</u> and <u>BVH-11</u> genes were expressed in <u>S.</u> pneumoniae. S. pneumoniae strain SP64 and SP63 were grown overnight at 37°C in 5% CO, on chocolate agar plates, bacteria were suspended in PBS and heat-killed at 56°C for 20 min. For the preparation of antigens, suspensions of S. 10 pneumoniae were treated with sample buffer containing SDS and 2-mercaptoethanol for 5 min at 100°C. Pneumococcal protein antigens were resolved by SDS-PAGE electrophoresis according to the method of Laemmli [Nature, 227, pp. 680-685 (1970)]. After SDS-PAGE, the proteins were transferred 15 electrophoretically from the gel to nitrocellulose paper by the method of Towbin [Proc. Natl. Acad. Sci. USA, 76, pp. 4350-4354 (1979)] and probed with mouse antiserum or monoclonal antibodies. The detection of antigens reactive with the antibodies was performed by indirect enzymeimmunoassay using conjugated-anti-mouse immunoglobulins and 20 a colour substrate. When antiserum raised to recombinant BVH-3 was tested against S. pneumoniae SP64 antigens, two reactive bands having apparent molecular masses of 127 kDa and 99 kDa were detected. Bands having the same apparent. molecular masses were also detected when Mabs H3-1-F9, H3-1-D4, H3-1-H12, H11-1-E7, H11-1-H10 and H11-1.1-G11 were used individually as immunological probes. In contrast, Mabs specific for the BVH-3 molecule detected the 127 kDa band only and Mabs specific for BVH-11 detected the 99 kDa 30 band only thus confirming the identity of the 127 and 99 kDa bands as BVH-3 and BVH-11, respectively. These studies provide evidence that BVH-3 and BVH-11 proteins are simultaneously present on S. pneumoniae. Moreover, the results are consistent with our previous observations that 35 BVH-3 and BVH-11 possess epitopes that are common to both proteins and epitopes that are exclusive to either protein.

In <u>S. pneumoniae</u> SP64, mature BVH-3, BVH-11 and BVH-11-2 are proteins of 1019, 821 and 819 amino acids with predicted molecular mass of 112.5 kDa, 92.4 kDa, and 91.7 kDa, respectively. Although there is a discrepancy between the molecular mass predicted from the sequence and the molecular mass calculated on SDS-PAGE, BVH-3 can be distinguished from BVH-11 by its higher molecular mass. Moreover, BVH-3 molecules from <u>S. pneumoniae</u> strain SP63 have an apparent molecular mass of 112 kDa in SDS-PAGE compared to 127 kDa for BVH-3 of SP64 strain. This data is consistent with the deletion of a stretch of 177 amino acid residues in BVH-3 of <u>S. pneumoniae</u> strain SP63.

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EXAMPLE 11

This example describes the protection conferred in experimental infection of mice vaccinated with recombinant BVH-3 or BVH-11 gene products.

Groups of 7 or 8 female BALB/c mice (Charles River) were immunized subcutaneously three times at three-week intervals with either affinity purified thioredoxin-

- 25 His•Tag-BVH-3M fusion protein, affinity purified thioredoxin-His•Tag-BVH-11M fusion protein or, as control, with QuilA adjuvant alone in PBS. Twelve to 14 days following the third immunization, the mice were challenged intravenously with <u>S. pneumoniae</u> WU2 strain or intranasally with P4241 strain. Samples of the <u>S. pneumoniae</u> challenge
 - with P4241 strain. Samples of the <u>S. pneumoniae</u> challenge inoculum were plated on chocolate agar plates to determine the CFU and to verify the challenge dose. The challenge dose was approximately 10° CFU. Deaths were recorded for a period of 14 days and on day 14 post-challenge, the
- 35 surviving mice were sacrificed and blood samples tested for

the presence of <u>S. pneumoniae</u> organisms. The survival data are shown in Tables 6 and 7.

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Table 6. Protection mediated by recombinant BVH-3M and BVH-11M proteins in experimental infection with virulent <u>S. pneumoniae</u> WU2

Experiment	Immunogen	Alive : dead	Median days alive
1	BVH-3M	8 : 0	>14
	none	0 : 8	1
2	BVH-11M	8 : 0	>14
	none	0:8	1

The number of mice alive: the number of mice dead on day 14 post-challenge.

Table 7. Protection mediated by recombinant BVH-3M and BVH-11M proteins in experimental pneumonia with virulent <u>S. pneumoniae</u> P4241

Experiment	Immunogen	Alive : dead	Median day alive
1	BVH-3M	6 : 1	>14
	none	1 : 7	4.5
2	BVH-3M	8 : 0	>14
	BVH-11M	8 : 0	>14
B 603	none	0 : 8	4

The number of mice alive: the number of mice dead on day 14 post-challenge.

All mice immunized with recombinant BVH-3M or BVH-11M

20 protein survived to infection with WU2 while none of the control mice given adjuvant alone survived. All except one mice immunized with recombinant BVH-3M or BVH-11M protein survived to infection with P4241 while only one control mice given adjuvant alone survived. All hemocultures from

surviving mice were negative at day 14 post-challenge. These results clearly indicate that both, BVH-3M and BVH-11M. elicit protective anti-pneumococcal immune responses in mice. The fact that these proteins are highly conserved among S. pneumoniae isolates emphasize the potential of BVH-3 and BVH-11 as universal vaccine candidates. Indeed, the BVH-3 and BVH-11 proteins from serogroup 6 S. pneumoniae strain SP64 elicited protection against pneumococcal infections with strains of different capsular serotypes.

Ideally, a vaccine that could protect against pneumococcal disease, could protect against meningitis, otitis media, bacteremia and pneumonia. BVH-3 and BVH-11 were protective against lethal systemic- and pneumonia-infection models thus suggesting that, in humans, BVH-3- and BVH11-proteinbased vaccines could reduce the incidence of a wide spectrum of disease caused by virtually all S. pneumoniae independently of the capsular serotype.

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Data from Tables 6 and 7 clearly demonstrate that BVH-3 and BVH-11 were, both, protection-eliciting molecules of S. pneumoniae. It was not known, however, whether protection can be mediated by specific sequences that were not shared on BVH-3 and BVH-11 molecules. Groups of female BALB/c mice (Charles River) were immunized subcutaneously three times at three-week intervals with either affinity purified thioredoxin-His•Tag- BVH-3AD, -BVH-3B or -BVH-3C fusion protein in presence of 15 μg of QuilA adjuvant (Cedarlane Laboratories Ltd, Hornby, Canada). Control mice were immunized with QuilA adjuvant alone in PBS or affinity purified thioredoxin-His•Tag or thioredoxin-His•Tag-fusion protein (His-Thio) in presence of QuilA.

To determine the protective ability of a set of truncated 35 proteins, termed NEW4, NEW5, NEW6, NEW7, NEW8, NEW9, NEW10,

NEW11, NEW14 and BVH-11B, groups of female BALB/c mice (Charles River) were immunized subcutaneously two times at three-week intervals with 25 μg of either affinity purified His•Tag-fusion protein in presence of 15 μg of QuilA

- adjuvant. Ten to 14 days following the last immunization, the mice were challenged with virulent <u>S. pneumoniae</u>. Our results indicate that, BVH-3B, a truncated BVH-3 molecule consisting of amino acids 512-1039, elicited protection against the mouse-virulent strains WU2 and P4241.
- 10 Similarly, BVH-11B, NEW4 and NEW5 molecules, three truncated BVH-11 molecules consisting of amino acids 354-840, amino acids 286-840 and amino acids 286-713, respectively, elicited protection against experiment intravenous challenge with WU2 and intranasal challenge
- with P4241. Moreover, vaccination with NEW10 and NEW14, consisting of amino acids 272-838 and amino acids 227-699 from BVH-11-2 molecule also resulted in protection against death with the pneumococcal strains. These results indicate that the region comprising 428 amino acids
- 20 extending from amino acids 286-713 and amino acids 272-699 on S. pneumoniae SP64 BVH-11 and BVH-11-2 protein sequences, respectively, contains protective epitopes.

 This region is highly conserved with a global 91% identity and 94% homology among thirteen BVH-11 protein sequences.

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Table 8. Evaluation of protection elicited by vaccination of mice with $\underline{BVH-3}$ and $\underline{BVH-11}$ gene products

		Challenge with WU2		Challenge with P4241	
Experiment	Immunogen	Alive : dead ^a	Median day	Alive : dead	Median day
			alive		alive
1 ⁵	None	0 : 8	1.5	1 : 7	4.5
	NEW4	8 : 0	>14	8 : 0	>14
	NEW5	8 : 0	>14	8 : 0	>14
	NEW7	0 : 8	2	0:8	5
	BVH-11M	8 : 0	>14	8:0	>14
2 ^b	None	0:8	1	0 : 8	4
	NEW5	8 : 0	>14	8 : 0	>14
	NEW8	0 : 8	1.5	0:8	5.5
	NEW9	3 : 5	3.5	2 : 6	7
	BVH-11M	8 : 0	>14	8 : 0	>14
3 th	None	0 : 8	1.	0 : 8	4
	NEW6	0 : 8	1	4:4	10.5°
	NEW10	8 : 0	>14	8:0	>14
	NEW11	0 : 8	1.5	1 : 7	6
	BVH-11M	8 : 0	>14	8 : 0	>14
4 ⁵	None	0:8	2	0 : 8	4
	BVH-11B	7 : 1	>14	8 : 0	>14
	NEW14	8 : 0	>14	8 : 0	>14
5	His-Thio	0 : 8	2		
	BVH-3AD .	1 : 7	2.5		• •
	BVH-3B	5 : 3	>14		
6	His-Thio	0 : 8	1		
	BVH-3C	0:8	1		

^{*} The number of mice alive : the number of mice dead on day 14 post-challenge.

⁵ b The WU2 challenge dose was 105 CFU.

[&]quot; Mice living longer than 14 days were assigned a survival time of 14 days for the determination of median values.

EXAMPLE 12

This example described the cloning and expression of a chimeric gene encoding for a chimeric polypeptide corresponding to the carboxy-terminal region of BVH-3 in fusion at the C' end to the carboxy-terminal region of BVH-11 and the additive protection observed after vaccination with a chimeric polypeptide.

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It is clear from the studies described above that BVH-3 and BVH-11 are serologically distinct molecules simultaneously present on S. pneumoniae. The results of immunological studies of mice indicate that both proteins are good 15 vaccine candidates. These proteins have the potential to provide protection against all pneumococci, regardless of serotype. Even though the two proteins share epitopes and sequences, they have different characteristics and may serve different biological functions. Thus, immunization 20 against the two proteins may provide a higher level of protection than that imparted by each individually. To examine this, several avenues where full-length or truncated BVH-3 and BVH-11 are administered in combination or in conjugation can be explored. Here we describe the genetic engineering of a BVH-3-BVH-11 fusion gene and protein, termed NEW12 (SEQ ID NO:76 and SEQ ID NO:58, respectively), and the potential use of NEW12 protein as a vaccine.

30 <u>BVH-3</u> and <u>BVH-11</u> gene fragments corresponding to the 3'end of the genes were amplified by PCR using pairs of oligonucleotides engineered to amplify fragments spanning nucleotides 1414 to 3117(SEQ ID NO: 1) and nucleotides 1060 to 2520 (SEQ ID NO: 3) from <u>S. pneumoniae</u> strain SP64 <u>BVH-3</u> and <u>BVH-11</u> genes, respectively. The primers used, HAMJ278

and HAMJ279; HAMJ282 and HAMJ283 had a restriction

endonuclease site at the 5' end, thereby allowing directional in-frame cloning of the amplified product into the digested pET21b(+) plasmid vector (Table 2). PCRamplified products were digested with restriction endonucleases and ligated to linearized plasmid pET21b(+) vector digested likewise. The resultant plasmid constructs were confirmed by nucleotide sequence analysis. recombinant pET21b(+) plasmid containing the NdeI-HindIII BVH-3 PCR product was linearized by digestion with the restriction enzymes HindIII and NotI for the in-frame 10 cloning of the HindIII-NotI DNA fragment obtained from the recombinant pET21(+) vector containing the BVH-11 gene fragment. Clones were first stabilized in $\underline{\text{E. coli}}$ DH5 α before introduction into \underline{E} . \underline{coli} BL21($\lambda DE3$) for expression of a chimeric pneumococcal protein molecule. The 15 recombinant chimeric polypeptide, termed NEW 12, was expressed as C-terminal fusion with an His-tag. expressed recombinant NEW 12 protein was purified from supernatant fractions obtained from centrifugation of sonicated IPTG-induced E. coli cultures using a His-Bind 20 metal chelation resin (QIAgen, Chatsworth, CA).

According to the same procedure described above, it is possible to construct other chimeric polypeptides, as a result of a simultaneous expression of New 1 and New 4, New 1 and New 5, New 1 and New 10, or New 1 and New 14. The construction can be with New 1 upstream or downstream of New 4, New 5, New 10, BVH-11B or New 14. It is also possible to construct other chimeric polypeptides as a result of a simultaneous expression of more than two fragments of either genes of BVH-3, BVH-11 or BVH-11-2.

Groups of 8 female BALB/c mice (Charles River) were immunized subcutaneously two times at three-week intervals with 25 μg of either affinity purified His•Tag-fusion NEW1,

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BVH-11B or NEW12 protein in presence of 15 μ g of QuilA adjuvant. Ten to 14 days following the last immunization, the mice were challenged with virulent S. pneumoniae. As demonstrated before, NEW1 and BVH-11B molecules comprising amino acids 472 to 1039 from BVH-3 protein and amino acids 354-840 from BVH-11 protein, respectively, correspond to portions of the proteins capable of eliciting a protective immune response. To determine if a chimeric polypeptide would significantly improve the protection compared with those seen for the individual counterparts, the challenge dose was adjusted in a manner that protection was not expected with NEW1 and BVH-11B molecules. Interestingly, the chimeric NEW12 protein, elicited protection against the mouse-virulent strains WU2 and P4241. Seven out of 8 mice immunized with NEW12 were still alive 10 days after the challenge while 28 out of 32 mice immunized with NEW1, BVH-11B, BVH-3M or adjuvant alone were dead by five days postchallenge. Thus, vaccination of mice with NEW12 provided the highest degree of protection against WU2 challenge. These results indicate that immunization with a chimeric polypeptide and possibly a combination of BVH-3 and BVH-11 gene products can provide additional protection to that obtained by administration of BVH-3 or BVH-11 antigens $\mathbf{alone.}$

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Table 9. Evaluation of protection elicited by vaccination of mice with the chimeric NEW12 molecule

Immunogen	Challenge with WU2		Challenge with P4241	
	Alive : dead ^a	Median day alive	Alive : dead	Median day alive
None	0:8	1	0 : 8	5
NEW1'	2 : 6	2	1 : 7	8
BVH-11B	1 : 7	3.5	8 : 0	>14
NEW12	6 : 2	>14	7 : 1	>14
BVH-3M	1 : 7	3	8 : 1	>14

EXAMPLE 13

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This example illustrates the identification of additional $\underline{BVH-3}$ and $\underline{BVH-11}$ related sequences in Streptococcus species other than \underline{S} . pneumoniae.

10 It was previously shown that BVH-3, BVH-11 and BVH-11-2 are a family of related proteins sharing common sequences. Homology searches were performed with the nucleotide sequence from the conserved region of these genes and compared with GenBank and EMBL sequences using FASTA. 15 most significant homology was observed with a 2.469-kb gene coding for a calculated 92-kDa protein (SEQ ID NO: 81) of unknown function in S. agalactiae also called group B streptococcus or GBS. The gene was designated BVH-71. protein demonstrating 99.2% identity and 99.5% similarity 20 with that of GBS was also identified in S. pyoqenes also called group A streptococcus or GAS (SEQ ID NO: 83). The 5' region of the BVH-71 sequences (SEQ ID NO: 80 and SEQ ID NO: 82), spanning nucleotides 1 to 717, demonstrated 58 and 60% identity with the conserved regions of BVH-3 (nucleotides 1 to 675) and <u>BVH-11</u> (nucleotides 1 to 684) genes respectively. The first 239 amino acids of the translated sequences of the GBS and GAS BVH-71 open reading frames are 51 and 54% identical to the first 225 and 228 amino acids of BVH-3 and BVH-11, respectively. In addition 30 to structural similarities, streptococcal BVH-3, BVH-11 and BVH-71 proteins also share antigenic epitopes. A 97-kDa band was revealed on Western blots of GAS or GBS whole

cells, using Mab H11-1.1-G11 reactive with the BVH-3 and

BVH-11 conserved regions. Similarly, GAS and GBS

recombinant BVH-71 proteins were detected in Western immunoblot analysis.

These results indicate that BVH-71, BVH-3 and BVH-11 proteins might share similar functions. Our results also suggest that BVH-71 proteins can be used as protein vaccine components of anti-streptococcus. In a further embodiment BVH-71 proteins can be used as protein vaccine components of anti-GAS or anti-GBS vaccines.

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What is claimed is:

 An isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide having a sequence chosen from: SEQ ID NOB: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

- 2. A polynucleotide according to claim 1, wherein said polynucleotide encodes a polypeptide having at least 95% identity to the second polypeptide.
- 3. An isolated polynucleotide encoding a polypeptide capable of generating antibodies having binding specificity for a polypeptide having a sequence chosen from: SEQ ID NOS: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.
- 4. An isolated polynucleotide that is complementary to the polynucleotide of claim 1.
- 5. An isolated polynucleotide that is complementary to the polynucleotide of claim 3.

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- 6. The polynucleotide of claim 1, wherein said polynucleotide is DNA.
- 7. The polynucleotide of claim 3, wherein said polynucleotide is DNA.
- 8. The polynucleotide of claim 1, wherein said polynucleotide is RNA.
- 9. The polynucleotide of claim 3, wherein said polynucleotide is RNA.

10. A vector comprising the polynucleotide of claim 1, wherein said DNA is operably linked to an expression control region.

- 11. A vector comprising the polynucleotide of claim 3, wherein said DNA is operably linked to an expression control region.
- 12. A host cell transfected with the vector of claim 10.
- 13. A host cell transfected with the vector of claim 11.
- 14. A process for producing a polypeptide comprising culturing a host cell according to claim 12 under conditions suitable for expression of said polypeptide.
- 15. A process for producing a polypeptide comprising culturing a host cell according to claim 13 under condition suitable for expression of said polypeptide.
- 16. An isolated polypeptide having at least 70% identity to a second polypeptide having an amino acid sequence chosen from: SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.
 - 17. An isolated polypeptide capable of generating antibodies having binding specificity for a second polypeptide having a sequence chosen from: SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

 $\label{eq:continuous} (x_1, x_2, \dots, x_n) = (x_1, \dots, x_n) + ($

18. An isolated polypeptide having an amino acid sequence chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

19. An isolated polypeptide according to claim 18, wherein the N-terminal Met residue is deleted.

- 20. An isolated polypeptide according to claim 18, wherein the secretory amino acid sequence is deleted.
- 21. A chimeric polypeptide comprising two or more polypeptides chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof; provided that the polypeptides or fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.
- 22. A chimeric polypeptide comprising two or more polypeptides chosen from SEQ ID NOs:10, 58, 60, 62, 64, 67, 68, 69, 72, 74, 77 or fragments, analogs or derivatives thereof; provided that the polypeptides or fragments, analogs or derivatives thereof are linked as to form a chimeric polypeptide.
- 23. A chimeric polypeptide of formula (I):

 A-(B)_m-(C)_m-D (I)

 Wherein;

m is 0 or 1,

n is 0 or 1,

A is chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof;

B is chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof;

C is chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55 to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof; and

D is chosen from SEQ ID NOs: 2, 4, 6, 8, 10, 14, 16, 55

to 75, 77 to 79, 81, 83 or fragments, analogs or derivatives thereof.

- 24. A chimeric polypeptide of formula (I):
 - $\mathbf{A} (\mathbf{B})_{\mathbf{n}} (\mathbf{C})_{\mathbf{n}} \mathbf{D} \qquad (\mathbf{I})$

Wherein;

m is 0 or 1,

n is 0 or 1,

A is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,

69, 72, 74, 77 or fragments, analogs or derivatives thereof:

B is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,

69, 72, 74, 77, or fragments, analogs or derivatives thereof;

C is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,

69, 72, 74, 77 or fragments, analogs or derivatives thereof; and

D is chosen from SEQ ID NOs :10, 58, 60, 62, 64, 67, 68,

69, 72, 74, 77 or fragments, analogs or derivatives thereof.

- 25. A vaccine composition comprising a polypeptide according
 to any one of claims 16 to 24 and a pharmaceutically
 acceptable carrier, diluent or adjuvant.
 - 26. A method for therapeutic or prophylactic treatment of meningitis, otitis media, bacteremia or pneumonia infection in an individual susceptible to meningitis, otitis media, bacteremia or pneumonia infection comprising administering to said individual a therapeutic or prophylactic amount of a composition according to claim 25.
 - 27. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an individual

susceptible to streptococcal infection comprising administering to said individual a therapeutic or prophylactic amount of a composition according to claim 25.

- 28. A method according to claim 26, wherein said individual is a mammal.
- 29. A method according to claim 27, wherein said individual is a human.
- 30. A method according to claim 22, wherein said bacterial infection is <u>S.pneumoniae</u>, group A streptococcus (pyogenes), group B streptococcus (GBS or agalactiae), dysgalactiae, uberis, nocardia or Staphylococcus aureus.
- 31. A method according to claim 26, wherein said bacterial infection is <u>S.pneumoniae</u>.
- 32. Use of a vaccine composition according to claim 25 for the prophylactic or therapeutic treatment of Streptococcal infection in an animal susceptible to or infected with streptococcal infection comprising administering to said animal a prophylactic or therapeutic amount of the composition.

					•	
ATGAAATTT	A GTAAAAAATA	TATAGCAGCT	GGATCAGCTG	TTATCGTATC	CTTGAGTCTA	60
TGTGCCTATC	3 CACTAAACCA	GCATCGTTCG	CAGGAAAATA	AGGACAATAA	TCGTGTCTCT	120
TATGTGGAT	G GCAGCCAGTC	: AAGTCAGAAA	AGTGAAAACT	TGACACCAGA	CCAGGTTAGC	180
CAGAAAGAAC	GAATTCAGGC	TGAGCAAATT	GTAATCAAAA	TTACAGATCA	GGGCTATGTA	240
ACGTCACACC	GTGACCACTA	TCATTACTAT	'AATGGGAAAG	TTCCTTATGA	TGCCCTCTTT	300
AGTGAAGAA	TCTTGATGAA	GGATCCAAAC	TATCAACTTA	AAGACGCTGA	TATTGTCAAT	360
GAAGTCAAGG	GTGGTTATAT	CATCAAGGTC	GATGGAAAAT	ATTATGTCTA	CCTGAAAGAT	420
GCAGCTCATO	CTGATAATGT	TCGAACTAAA	GATGAAATCA	ATCGTCAAAA	ACAAGAACAT	480
GTCAAAGATA	ATGAGAAGGT	TAACTCTAAT	GTTGCTGTAG	CAAGGTCTCA	GGGACGATAT	540
ACGACAAATC	ATGGTTATGT	CTTTAATCCA	GCTGATATTA	TCGAAGATAC	GGGTAATGCT	600
TATATCGTTC	CTCATGGAGG	TCACTATCAC	TACATTCCCA	AAAGCGATTT	ATCTGCTAGT	660
GAATTAGCAG	CAGCTAAAGC	ACATCTGGCT	GGAAAAAATA	TGCAACCGAG	TCAGTTAAGC	720
TATTCTTCAA	CAGCTAGTGA	CAATAACACG	CAATCTGTAG	CAAAAGGATC	AACTAGCAAG	780
CCAGCAAATA	AATCTGAAAA	TCTCCAGAGT	CTTTTGAAGG	AACTCTATGA	TTCACCTAGC	840
GCCCAACGTT	' ACAGTGAATC	AGATGGCCTG	GTCTTTGACC	CTGCTAAGAT	TATCAGTCGT	900
ACACCAAATG	GAGTTGCGAT	TCCGCATGGC	GACCATTACC	ACTTTATTCC	TTACAGCAAG	960
CTTTCTGCTT	' TAGAAGAAAA	GATTGCCAGA	ATGGTGCCTA	TCAGTGGAAC	TGGTTCTACA	1020
GTTTCTACAA	ATGCAAAACC	TAATGAAGTA	GTGTCTAGTC	TAGGCAGTCT	TTCAAGCAAT	1080
CCTTCTTCTT	TAACGACAAG	TAAGGAGCTC	TCTTCAGCAT	CTGATGGTTA	יי א איזיירייייייייי מיי	1140
CCAAAAGATA	TCGTTGAAGA	AACGGCTACA	GCTTATATTG	TAAGACATGG	TGATCATTTC	
CATTACATTC	CAAAATCAAA	TCAAATTGGG	CAACCGACTC	TTCCAAACAA	TAGTCTAGCA	1200 1260
ACACCTTCTC	CATCTCTTCC	AATCAATCCA	GGAACTTCAC	ATGAGAAACA	TGAAGAAGAT	
GGATACGGAT	TTGATGCTAA	TCGTATTATC	GCTGAAGATG	AATCAGGTTT	TGTCATGAGT	1320 1380
CACGGAGACC	ACAATCATTA	TTTCTTCAAG	AAGGACTTGA	CAGAAGAGCA	AATTAAGGCT	1440
GCGCAAAAAC	ATTTAGAGGA	AGTTAAAACT	AGTCATAATG	GATTAGATTC	TTTGTCATCT	1500
CATGAACAGG	ATTATCCAGG	TAATGCCAAA	GAAATGAAAG	ATTTAGATAA	AAAAATCGAA	1560
GAAAAAATTG	CTGGCATTAT	GAAACAATAT	GGTGTCAAAC	GTGAAAGTAT	TGTCGTGAAT	1620
AAAGAAAAA	ATGCGATTAT	TTATCCGCAT	GGAGATCACC	ATCATGCAGA	TCCGATTGAT	1680
GAACATAAAC	CGGTTGGAAT	TGGTCATTCT	CACAGTAACT	ATGAACTGTT	TAAACCCGAA	1740
GAAGGAGTTG	CTAAAAAAGA	AGGGAATAAA	GTTTATACTG	GAGAAGAATT	AACGAATGTT	1800
GTTAATTTGT	TAAAAAATAG	TACGTTTAAT	AATCAAAACT	TTACTCTAGC	CAATGGTCAA	1860
AAACGCGTTT	CTTTTAGTTT	TCCGCCTGAA	TTGGAGAAAA	AATTAGGTAT	ለ ተግርንፐልፐልፈብ	1920
GTAAAATTAA	TAACACCAGA	TGGAAAAGTA	TTGGAGAAAG	TATCTGGTAA	AGTATTTGGA	1980
GAAGGAGTAG	GGAATATTGC	AAACTTTGAA	TTAGATCAAC	CTTATTTACC	AGGACAAACA	2040
TTTAAGTATA	CTATCGCTTC	AAAAGATTAT	CCAGAAGTAA	GTTATGATGG	TACATTTACA	2100
GTTCCAACCT	CTTTAGCTTA	CAAAATGGCC	AGTCAAACGA	TTTTCTATCC	ጥጥሮሮልጥሮሮል · ·	2160
GGGGATACTT	ATTTAAGAGT	GAACCCTCAA	TTTGCAGTGC	CTAAAGGAAC	ТСАТССТТТА	2220
GTCAGAGTGT	TTGATGAATT	TCATGGAAAT	GCTTATTTAG	AAAATAACTA	TAAAGTTGGT	2280
GAAATCAAAT	TACCGATTCC	GAAATTAAAC	CAAGGAACAA	CCAGAACGGC :	ממדמממסטט	2340
ATTCCTGTAA	CCTTCATGGC	AAATGCTTAT	TTGGACAATC	AATCGACTTA	TATTGTGGAA	2400
GTACCTATCT	TGGAAAAAGA	AAATCAAACT	GATAAACCAA	GTATTCTACC	ACAATTTAAA	2460
AGGAATAAAG	CACAAGAAAA	CTCAAAACTT	GATGAAAAGG	TAGAAGAACC .	AAAGACTAGT	2520
GAGAAGGTAG	AAAAAGAAAA	ACTTTCTGAA	ACTGGGAATA	GTACTAGTAA	TTCAACGTTA	2580
GAAGAAGTTC	CTACAGTGGA	TCCTGTACAA	GAAAAAGTAG	CAAAATTTGC	TGAAAGTTAT	2640
GGGATGAAGC	TAGAAAATGT	CTTGTTTAAT	ATGGACGGAA	CAATTGAATT .	ATATTTACCA	2700
TCAGGAGAAG	TCATTAAAAA	GAATATGGCA	GATTTTACAG	GAGAAGCACC	TOAGGAAAT	2760
GGTGAAAATA	AACCATCTGA	AAATGGAAAA	GTATCTACTG	GAACAGTTGA	GAACCAACCA	2820
ACAGAAAATA	AACCAGCAGA	TTCTTTACCA	GAGGCACCAA	ACGAAAAACC	TGT እ እ አ CC እ	2880
GAAAACTCAA	CGGATAATGG	AATGTTGAAT	CCAGAAGGGA	ATGTGGGGAG '	アにないつつならて	2940
TIAGATCCAG	CATTAGAGGA	AGCTCCAGCA	GTAGATCCTG	TACAAGAAAA	Απτασαακα	3000
TITACAGCTA	GTTACGGATT	AGGCTTAGAT	AGTGTTATAT 🕆	TCAATATGGA '	TGGAACGATT	3060
GAATTAAGAT (SEQ ID NO:	TGCCAAGTGG	AGAAGTGATA	AAAAAGAATT	TATCTGATTT	CATAGCGTAA	3120
PER IN MOI	1)	FIGU	JRE 1			

MKFSKKYIAA	GSAVIVSLSL	CAYALNOHRS	QENKDNNRVS	YVDGSQSSQK		50
SENLTPDQVS	QKEGIQAEQI	VIKITDQGYV	TSHGDHYHYY	NGKVPYDALF		100
SEELLMKDPN	YQLKDADIVN	EVKGGYIIKV	DGKYYVYLKD	AAHADNVRTK		150
DEINRQKQEH	VKDNEKVNSN	VAVARSQGRY	TTNDGYVFNP	ADIIEDTGNA		200
YIVPHGGHYH	YIPKSDLSAS	ELAAAKAHLA	GKNMQPSQLS	YSSTASDNNT		250
QSVAKGSTSK	PANKSENLQS	LLKELYDSPS	AQRYSESDGL	VFDPAKIISR		300
TPNGVAIPHG			MVPISGTGST			350
VSSLGSLSSN	PSSLTTSKEL	SSASDGYIFN	PKDIVEETAT	AYIVRHGDHF		400
HYIPKSNQIG	QPTLPNNSLA	TPSPSLPINP	GTSHEKHEED	GYGFDANRII		450
AEDESGFVMS	HGDHNHYFFK	KDLTEEQIKA	AQKHLEEVKT	SHNGLDSLSS		500
HEQDYPGNAK	EMKDLDKKIE	EKIAGIMKQY	GVKRESIVVN	KEKNAIIYPH		550
GDHHHADPID	EHKPVGIGHS	HSNYELFKPE	EGVAKKEGNK	VYTGEELTNV		600
VNLLKNSTFN	NQNFTLANGQ	KRVSFSFPPE	LEKKLGINML	VKLITPDGKV		650
LEKVSGKVFG	EGVGNIANFE	LDQPYLPGQT	FKYTIASKDY	PEVSYDGTFT		700
VPTSI.AYKMA	SQTIFYPFHA	GDTYLRVNPQ	FAVPKGTDAL	VRVFDEFHGN		750
AYLENNYKVG	EIKLPIPKLN	QGTTRTAGNK	IPVTFMANAY	LDNQSTYIVE		800
VPILEKENQT	DKPSILPQFK	RNKAQENSKL	DEKVEEPKTS	EKVEKEKLSE		850
TGNSTSNSTL	EEVPTVDPVQ	EKVAKFAESY	GMKLENVLFN	MDGTIELYLP		900
SGEVIKKNMA	DFTGEAPQGN	GENKPSENGK	VSTGTVENQP	TENKPADSLP		950
EAPNEKPVKP	ENSTDNGMLN	PEGNVGSDPM	LDPALEEAPA	VDPVQEKLEK		1000
FTASYGLGLD	SVIFNMDGTI	ELRLPSGEVI	KKNLSDFIA	SEO ID NO:	21	1039

FIGURE 2

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and a contract of the contract

ATCA A A ATCA		mcm> ccmccc				
COTTATOR	TRAAAAAATA	TCTAGCTGGG	TCAGTAGCTA	CACTTGTTTT	AAGTGTCTGT	60
DETINICANO	ANGENTIGO	TCAAGCTCAA	ACTGTAAAAG	AAAATAATCG	TGTTTCCTAT	120
COTTONICON	MACAAGCGAC	GCAAAAAACG	GAGAATITGA	CTCCTGATGA	GGTTAGCAAG	180
TOTOLOGO	TCAACGCCGA	ACAAATCGTC	ATCAAGATTA	CGGATCAAGG	TTATGTGACC	240
TCTCATGGAG	ACCATTATCA	TTACTATAAT	GGCAAGGTCC	CTTATGATGC	CATCATCAGT	300
GAAGAGCTCC	TCATGAAAGA	TCCGAATTAT	CAGTTGAAGG	ATTCAGACAT	TGTCAATGAA	360
ATCAAGGGTG	GTTATGTCAT	' TAAGGTAAAC	GGTAAATACT	ATGTTTACCT	TAAGGATGCA	420
GCTCATGCGG	ATAATGTCCG	TACAAAAGAA	GAAATCAATC	GGCAAAAACA	AGAACATAGT	480
CAGCATCGTG	AAGGAGGGAC	TTCAGCAAAC	GATGGTGCGG	TAGCCTTTGC	ACGTTCACAG	540
GGACGCTACA	CCACAGATGA	TGGTTATATC	TTCAATGCAT	CTGATATCAT	CGAAGATACG	600
GGCGATGCCT	ATATCGTTCC	TCATGGAGAT	CATTACCATT	ACATTCCTAA	GAATGAGTTA	660
TCAGCTAGCG	AGTTGGCTGC	TGCAGAAGCC	TTCCTATCTG	GTCGGGAAAA	TCTGTCAAAT	720
TTAAGAACCT	' ATCGCCGACA	AAATAGCGAT	AACACTCCAA	GAACAAACTG	GGTACCTTCT	780
GTAAGCAATC	CAGGAACTAC	AAATACTAAC	ACAAGCAACA	ACAGCAACAC	TAACAGTCAA	840
GCAAGTCAAA	GTAATGACAT	TGATAGTCTC	TTGAAACAGC	TCTACAAACT	GCCTTTGAGT	900
CAACGCCATG	TAGAATCTGA	TGGCCTTATT	TTCGACCCAG	CGCAAATCAC	AAGTCGAACC	960
GCCAGAGGTG	TAGCTGTCCC	TCATGGTAAC	CATTACCACT	TTATCCCTTA	TGAACAAATG	1020
TCTGAATTGG	AAAAACGAAT	TGCTCGTATT	ATTCCCCTTC	GTTATCGTTC	AAACCATTGG	1080
GTACCAGATT	CAAGACCAGA	AGAACCAAGT	CCACAACCGA	CTCCAGAACC	TAGTCCAAGT	1140
CCGCAACCTG	CACCAAATCC	TCAACCAGCT	CCAAGCAATC	CAATTGATGA	GAAATTGGTC	1200
AAAGAAGCTG	TTCGAAAAGT	AGGCGATGGT	TATGTCTTTG	AGGAGAATGG	AGTTTCTCGT	1260
TATATCCCAG	CCAAGAATCT	TTCAGCAGAA	ACAGCAGCAG	GCATTGATAG	CAAACTGGCC	1320
AAGCAGGAAA	GTTTATCTCA	TAAGCTAGGA	GCTAAGAAAA	CTGACCTCCC	ATCTAGTGAT	1380
CGAGAATTTT	ACAATAAGGC	TTATGACTTA	CTAGCAAGAA	TTCACCAAGA	TTTACTTGAT	1440
AATAAAGGTC	GACAAGTTGA	TTTTGAGGCT	TTGGATAACC	TGTTGGAACG	ACTCAAGGAT	1500
GTCTCAAGTG	ATAAAGTCAA	GTTAGTGGAT	GATATTCTTG	CCTTCTTAGC	TCCGATTCGT	1560
CATCCAGAAC	GTTTAGGAAA	ACCAAATGCG	CAAATTACCT	ACACTGATGA	TGAGATTCAA	1620
GTAGCCAAGT	TGGCAGGCAA	GTACACAACA	GAAGACGGTT	ATATCTTTGA	TCCTCGTGAT	1680
ATAACCAGTG	ATGAGGGGGA	TGCCTATGTA	ACTCCACATA	TGACCCATAG	CCACTGGATT	1740
AAAAAAGATA	GTTTGTCTGA	AGCTGAGAGA	GCGGCAGCCC	AGGCTTATGC	TAAAGAGAAA	1800
GGTTTGACCC	CTCCTTCGAC	AGACCATCAG	GATTCAGGAA	ATACTGAGGC	AAAAGGAGCA	1860
GAAGCTATCT	ACAACCGCGT	GAAAGCAGCT	AAGAAGGTGC	CACTTGATCG	TATGCCTTAC	1920
AATCTTCAAT	ATACTGTAGA	AGTCAAAAAC	GGTAGTTTAA	TCATACCTCA	TTATGACCAT	1980
TACCATAACA	TCAAATTTGA	GTGGTTTGAC	GAAGGCCTTT	ATGAGGCACC	TAAGGGGTAT	2040
ACTCTTGAGG	ATCTTTTGGC	GACTGTCAAG	TACTATGTCG	AACATCCAAA	CGAACGTCCG	2100
CATTCAGATA	ATGGTTTTGG	TAACGCTAGC	GACCATGTTC	AAAGAAACAA	AAATGGTCAA	2160
GCTGATACCA	ATCAAACGGA	AAAACCAAGC	GAGGAGAAAC	CTCAGACAGA	AAAACCTGAG	2220
GAAGAAACCC	CTCGAGAAGA	GAAACCACAA	AGCGAGAAAC	CAGAGTCTCC	AAAACCAACA	2280
GAGGAACCAG	AAGAAGAATC	ACCAGAGGAA	TCAGAAGAAC	CTCAGGTCGA	GACTGAAAAG	2340
GTTGAAGAAA	AACTGAGAGA	GGCTGAAGAT	TTACTTGGAA	AAATCCAGGA	TCCAATTATC	2400
AAGTCCAATG	CCAAAGAGAC	TCTCACAGGA	TTAAAAAATA	ATTTACTATT	TGGCACCCAG	2460
GACAACAATA	CTATTATGGC	AGAAGCTGAA	AAACTATTGG	CTTTATTAAA	GGAGAGTAAG	2520
	ID NO: 3)					2523

MKINKKYLAG	SVATLVLSVC	AYELGLHQAQ	TVKENNRVSY	IDGKQATQKT		50
ENLTPDEVSK	REGINAEQIV	IKITDQGYVT	SHGDHYHYYN	GKVPYDAIIS		100
EELLMKDPNY	QLKDSDIVNE	IKGGYVIKVN	GKYYVYLKDA	AHADNVRTKE		150
EINRQKQEHS	QHREGGTSAN	DGAVAFARSQ	GRYTTDDGYI	FNASDIIEDT		200
GDAYIVPHGD	HYHYIPKNEL	SASELAAAEA	FLSGRENLSN	LRTYRRQNSD		250
NTPRTNWVPS	VSNPGTTNTN	TSNNSNTNSQ	ASQSNDIDSL	LKQLYKLPLS		300
QRHVESDGLI	FDPAQITSRT	ARGVAVPHGN	HYHFIPYEQM	SELEKRIARI		350
IPLRYRSNHW	VPDSRPEEPS	PQPTPEPSPS	PQPAPNPQPA	PSNPIDEKLV		400
KEAVRKVGDG	YVFEENGVSR	YIPAKNLSAE	TAAGIDSKLA	KQESLSHKLG		450
AKKTDLPSSD	REFYNKAYDL	LARIHQDLLD	NKGRQVDFEA	LDNLLERLKD		500
VSSDKVKLVD	DILAFLAPIR	HPERLGKPNA	QITYTDDEIQ	VAKLAGKYTT		550
EDGYIFDPRD	ITSDEGDAYV	TPHMTHSHWI	KKDSLSEAER	AAAQAYAKEK		600
GLTPPSTDHQ	DSGNTEAKGA	EAIYNRVKAA	KKVPLDRMPY	NLQYTVEVKN		650
GSLIIPHYDH	YHNIKFEWFD	EGLYEAPKGY	TLEDLLATVK	YYVEHPNERP		700
HSDNGFGNAS	DHVQRNKNGQ	ADTNQTEKPS	EEKPQTEKPE	EETPREEKPQ		750
SEKPESPKPT	EEPEEESPEE	SEEPQVETEK	VEEKLREAED	LLGKIQDPII		800
KSNAKETLTG	LKNNLLFGTO	DNNTIMAEAE	KLLALLKESK	(SEO ID NO:	4)	840

FIGURE 4

ATGGAGAATA	TAGACATGTT	TAAATCAAAT	CATGAGCGAA	GAATGCGTTA	TTCCATTCGT	60	
AAATTTAGTG	TAGGAGTAGC	TAGCGTAGCT	GTTGCCAGTC	TTTTTATGGG	AAGTGTTGTA	120	
CATGCGACAG	AGAAAGAGGG	AAGTACCCAA	GCAGCCACTT	CTTTTAATAG	GGGAAATGGA	180	
AGTCAGGCAG	AACAACGTGG	AGAACTCGAT	TTAGAACGAG	ATAAGGCAAT	GAAAGCGGTC	240	
AGTGAATATG	TAGGAAAAAT	GGTGAGAGAT	GCCTATGTAA	AATCAGATAG	AAAACGACAT	300	
AAAAATACTG	TAGCTCTAGT	TAACCAGTTG	GGAAACATTA	AGAACAGGTA	TTTGAATGAA	360	
ATAGTTCATT	CAACCTCAAA	AAGCCAACTA	CAGGAACTGA	TGATGAAGAG	TCAATCAGAA	420	
GTAGATGAAG	CTGTGTCTAA	ATTTGAAAAG	GACTCATTTT	CTTCGTCAAG	TTCAGGATCC	480	
TCCACTAAAC	CAGAAACTCC	GCAGCCGGAA	AATCCAGAGC	ATCAAAAACC	AACAACTCCA	540	
TCTCCGGATA	CCAAACCAAG	CCCTCAACCA	GAAGGCAAGA	AACCAAGCGT	ACCAGACATT	600	
AATCAGGAAA	AAGAAAAAGC	TAAGCTTGCT	GTAGTAACCT	ACATGAGCAA	GATTTTAGAT	660	
GATATACAAA	AACATCATCT	GCAGAAAGAA	AAACATCGTC	AGATTGTTGC	TCTTATTAAG	720	
GAGCTTGATG	AGCTTAAAAA	GCAAGCTCTT	TCTGAAATTG	ATAATGTAAA	TACCAAAGTA	780	
GAAATTGAAA	ATACAGTCCA	CAAGATATTT	GCAGACATGG	ATGCAGTTGT	GACTAAATTC	840	and the property of the party of the
AAAAAAGGCT	TAACTCAGGA	CACACCAAAA	GAACCAGGTA	ACAAAAAACC	ATCTGCTCCA	900	
AAACCAGGTA	TGCAACCAAG	TCCTCAACCA	GAGGTTAAAC	CGCAGCTGGA	AAAACCAAAA	960	
CCAGAGGTTA	AACCGCAACC	AGAAAAACCA	AAACCAGAGG	TTAAACCGCA	GCCGGAAAAA	1020	
CCAAAACCAG	AGGTTAAACC	GCAGCCGGAA	AAACCAAAAC	CAGAGGTTAA	ACCGCAGCCG	1080	
GAAAAACCAA	AACCAGAGGT	TAAACCGCAG	CCGGAAAAAC	CAAAACCAGA	GGTTAAACCG	1140	
CAGCCGGAAA	AACCAAAACC	AGAGGTTAAA	CCGCAGCCGG	AAAAACCAAA	ACCAGAGGTT	1200	
AAACCGCAGC	CGGAAAAACC	AAAACCAGAG	GTTAAACCGC	AGCCGGAAAA	ACCAAAACCA	1260	
GAGGTTAAAC	CGCAGCCGGA	AAAACCAAAA	CCAGAGGTTA	AACCGCAACC	AGAAAAACCA	1320	
AAACCAGAGG	TTAAACCGCA	ACCAGAAAAA	CCAAAACCAG	ATAATAGCAA	GCCACAAGCA	1380	
GATGATAAGA	AGCCATCAAC	TACAAATAAT	TTAAGCAAGG	ACAAGCAACC	TTCTAACCAA	1440	
GCTTCAACAA	ACGAAAAAGC	AACAAATAAA	CCGAAGAAGT	CATTGCCATC	AACTGGATCT	1500	
ATTTCAAATC	TAGCACTTGA	AATTGCAGGT	CTTCTTACCT	TGGCGGGGGC	AACCATTCTT	1560	
GCTAAGAAAA	GAATGAAATA	G (SEQ ID	NO: 5)			1581	

MENIDMFKSN	HERRMRYSIR	KFSVGVASVA	VASLFMGSVV	HATEKEGSTQ	50
			SEYVGKMVRD		100
			QELMMKSQSE		150
DSFSSSSSSS	STKPETPQPE	NPEHQKPTTP	SPDTKPSPQP	EGKKPSVPDI	200
NQEKEKAKLA	VVTYMSKILD	DIQKHHLQKE	KHRQIVALIK	ELDELKKQAL	250
SEIDNVNTKV	EIENTVHKIF	ADMDAVVTKF	KKGLTQDTPK	EPGNKKPSAP	300
			KPEVKPQPEK		350
KPKPEVKPQP	EKPKPEVKPQ	PEKPKPEVKP	QPEKPKPEVK	PQPEKPKPEV	400
KPQPEKPKPE	VKPQPEKPKP	EVKPQPEKPK	PEVKPQPEKP	KPEVKPQPEK	450
PKPDNSKPQA	DDKKPSTTNN	LSKDKQPSNQ	ASTNEKATNK	PKKSLPSTGS	500
ISNLALEIAG	LLTLAGATIL	AKKRMK	(SEQ ID NO): 6)	526

FIGURE 6

ATGAAATTTA	GTAAAAAATA	TATAGCAGCT	GGATCAGCTG	TTATCGTATC	CTTGAGTCTA	60
	CACTAAACCA			AGGACAATAA	TCGTGTCTCT	120
TATGTGGATG	GCAGCCAGTC	AAGTCAGAAA	AGTGAAAACT	TGACACCAGA	CCAGGTTAGC	180
CAGAAAGAAG	GAATTCAGGC	TGAGCAAATT	GTAATCAAAA	TTACAGATCA	GGGCTATGTA	240
ACGTCACACG	GTGACCACTA	TCATTACTAT	AATGGGAAAG	TTCCTTATGA		300
AGTGAAGAAC	TCTTGATGAA	GGATCCAAAC	TATCAACTTA	AAGACGCTGA	TATTGTCAAT	360
GAAGTCAAGG	GTGGTTATAT	CATCAAGGTC	GATGGAAAAT	ATTATGTCTA	CCTGAAAGAT	420
GCAGCTCATG	CTGATAATGT	TCGAACTAAA	GATGAAATCA	ATCGTCAAAA	ACAAGAACAT	480
GTCAAAGATA				CAAGGTCTCA		540
ACGACAAATG	ATGGTTATGT					600
TATATCGTTC	CTCATGGAGG	TCACTATCAC	TACATTCCCA	AAAGCGATTT	ATCTGCTAGT	660
GAATTAGCAG	CAGCTAAAGC	ACATCTGGCT	GGAAAAAATA	TGCAACCGAG	TCAGTTAAGC	720
TATTCTTCAA	CAGCTAGTGA	CAATAACACG	CAATCTGTAG	CAAAAGGATC	AACTAGCAAG	780
CCAGCAAATA	AATCTGAAAA	TCTCCAGAGT	CTTTTGAAGG	AACTCTATGA	TTCACCTAGC	840
GCCCAACGTT	ACAGTGAATC	AGATGGCCTG	GTCTTTGACC	CTGCTAAGAT	TATCAGTCGT	900
ACACCAAATG	GAGTTGCGAT	TCCGCATGGC	GACCATTACC	ACTTTATTCC	TTACAGCAAG	960
CTTTCTGCTT	TAGAAGAAAA	GATTGCCAGA	ATGGTGCCTA	TCAGTGGAAC	TGGTTCTACA	1020
GTTTCTACAA	ATGCAAAACC	TAATGAAGTA	GTGTCTAGTC	TAGGCAGTCT	TTCAAGCAAT	1080
CCTTCTTCTT	TAACGACAAG	TAAGGAGCTC	TCTTCAGCAT	CTGATGGTTA	TATTTTTAAT	1140
CCAAAAGATA	TCGTTGAAGA	AACGGCTACA	GCTTATATTG	TAAGACATGG	TGATCATTTC	1200
	CAAAATCAAA					1260
ACACCTTCTC	CATCTCTTCC	AATCAATCCA	GGAACTTCAC	ATGAGAAACA	TGAAGAAGAT	1320
					TGTCATGAGT	1380
	ACAATCATTA	TTTCTTCAAG	AAGGACTTGA	CAGAAGAGCA	AATTAAGGTG	1440
CGCAAAAACA	TTTAG (SE	Q ID NO: 7)				1455

MKFSKKYIAA	GSAVIVSLSL	CAYALNQHRS	QENKDNNRVS	YVDGSQSSQK	50
			TSHGDHYHYY		100
			DGKYYVYLKD		150
DEINRQKQEH	VKDNEKVNSN	VAVARSQGRY	TTNDGYVFNP	ADIIEDTGNA	200
YIVPHGGHYH	YIPKSDLSAS	ELAAAKAHLA	GKNMQPSQLS	YSSTASDNNT	250
QSVAKGSTSK	PANKSENLQS	LLKELYDSPS	AQRYSESDGL	VFDPAKIISR	300
TPNGVAIPHG	DHYHFIPYSK	LSALEEKIAR	MVPISGTGST	VSTNAKPNEV	350
VSSLGSLSSN	PSSLTTSKEL	SSASDGYIFN	PKDIVEETAT	AYIVRHGDHF	400
HYIPKSNQIG	OPTLPNNSLA	TPSPSLPINP	GTSHEKHEED	GYGFDANRII	450
AEDESGFVMS	HGDHNHYFFK	KDLTEEQIKV	RKNI (SEÇ	ID NO: 8)	484

FIGURE 8

ATGAAAGATT	TAGATAAAAA	AATCGAAGAA	AAAATTGCTG	GCATTATGAA	ACAATATGGT	60
GTCAAACGTG	AAAGTATTGT	CGTGAATAAA	GAAAAAAATG	CGATTATTTA	TCCGCATGGA	120
GATCACCATC	ATGCAGATCC	GATTGATGAA	CATAAACCGG	TTGGAATTGG	TCATTCTCAC	180
AGTAACTATG	AACTGTTŢAA	ACCCGAAGAA	GGAGTTGCTA	AAAAAGAAGG	GAATAAAGTT	240
TATACTGGAG	AAGAATTAAC	GAATGTTGTT	AATTTGTTAA	AAAATAGTAC	GTTTAATAAT	300
CAAAACTTTA	CTCTAGCCAA	TGGTCAAAAA	CGCGTTTCTT	TTAGTTTTCC	GCCTGAATTG	360
GAGAAAAAAT	TAGGTATCAA	TATGCTAGTA	AAATTAATAA	CACCAGATGG	AAAAGTATTG	420
GAGAAAGTAT	CTGGTAAAGT	ATTTGGAGAA	GGAGTAGGGA	ATATTGCAAA	CTTTGAATTA	480
GATCAACCTT	ATTTACCAGG	ACAAACATTT	AAGTATACTA	TCGCTTCAAA	AGATTATCCA	540
GAAGTAAGTT	ATGATGGTAC	ATTTACAGTT		TAGCTTACAA		600
CAAACGATTT	TCTATCCTTT	CCATGCAGGG	GATACTTATT	TAAGAGTGAA	CCCTCAATTT	660
GCAGTGCCTA	AAGGAACTGA	TGCTTTAGTC	AGAGTGTTTG	ATGAATTTCA	TGGAAATGCT	720
TATTTAGAAA	ATAACTATAA	AGTTGGTGAA	ATCAAATTAC	CGATTCCGAA	ATTAAACCAA	780
GGAACAACCA	GAACGGCCGG	AAATAAAATT	CCTGTAACCT	TCATGGCAAA	TGCTTATTTG	840
GACAATCAAT	CGACTTATAT	TGTGGAAGTA	CCTATCTTGG	AAAAAGAAAA	TCAAACTGAT	900
AAACCAAGTA	TTCTACCACA	ATTTAAAAGG	AATAAAGCAC	AAGAAAACTC	AAAACTTGAT	960
GAAAAGGTAG	AAGAACCAAA	GACTAGTGAG	AAGGTAGAAA	AAGAAAAACT	TTCTGAAACT	1020
GGGAATAGTA	CTAGTAATTC	AACGTTAGAA	GAAGTTCCTA	CAGTGGATCC	TGTACAAGAA	1080
AAAGTAGCAA	AATTTGCTGA	AAGTTATGGG	ATGAAGCTAG	AAAATGTCTT	GTTTAATATG	1140
GACGGAACAA	TTGAATTATA	TTTACCATCA	GGAGAAGTCA	TTAAAAAGAA	TATGGCAGAT	1200
TTTACAGGAG	AAGCACCTCA	AGGAAATGGT	GAAAATAAAC	CATCTGAAAA	TGGAAAAGTA	1260
TCTACTGGAA	CAGTTGAGAA	CCAACCAACA	GAAAATAAAC	CAGCAGATTC	TTTACCAGAG	1320
GCACCAAACG	AAAAACCTGT	AAAACCAGAA	AACTCAACGG	ATAATGGAAT	GTTGAATCCA	1380
GAAGGGAATG	TGGGGAGTGA	CCCTATGTTA	GATCCAGCAT	TAGAGGAAGC	TCCAGCAGTA	1440
GATCCTGTAC	AAGAAAAATT	AGAAAAATTT	ACAGCTAGTT	ACGGATTAGG	CTTAGATAGT	1500
GTTATATTCA	ATATGGATGG	AACGATTGAA.	TTAAGATTGC	CAAGTGGAGA	AGTGATAAAA	1560
	CTGATTTCAT		(SEQ ID NO			1587

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PCT/CA99/01218 MKDLDKKIEE KIAGIMKQYG VKRESIVVNK EKNAIIYPHG DHHHADPIDE 50 HKPVGIGHSH SNYELFKPEE GVAKKEGNKV YTGEELTNVV NLLKNSTFNN 100 QNFTLANGQK RVSFSFPPEL EKKLGINMLV KLITPDGKVL EKVSGKVFGE 150 GVGNIANFEL DQPYLPGQTF KYTIASKDYP EVSYDGTFTV PTSLAYKMAS 200 QTIFYPFHAG DTYLRVNPQF AVPKGTDALV RVFDEFHGNA YLENNYKVGE 250 IKLPIPKLNQ GTTRTAGNKI PVTFMANAYL DNQSTYIVEV PILEKENQTD 300 KPSILPQFKR NKAQENSKLD EKVEEPKTSE KVEKEKLSET GNSTSNSTLE 350 EVPTVDPVQE KVAKFAESYG MKLENVLFNM DGTIELYLPS GEVIKKNMAD 400 FTGEAPQGNG ENKPSENGKV STGTVENQPT ENKPADSLPE APNEKPVKPE 450 NSTDNGMLNP EGNVGSDPML DPALEEAPAV DPVQEKLEKF TASYGLGLDS 500 VIFNMDGTIE LRLPSGEVIK KNLSDFIA (SEQ ID NO: 10) 528

FIGURE 10

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```
BVH3 WU2
                  1 CAYALNOHRSQENKDNNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
 BVH3 RX1
                  1 CAYALNOHRSQENKDNNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
BVH3 JNR7/87
                  1 CAYALNQHRSQENKDNNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
BVH3 SP64
                  1 CAYALNQHRSQENKDNNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
BVH3 P4241
                  1 CAYALNOHRSQENKONNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
BVH3 A66
                  1 CAYALNQHRSQENKDNNRVSYVDGSQSSQKSENLTPDQVSQKEGIQAEQIVIKITDQGYV
                                                                                   60
BVH3 WU2
                 61 TSHCDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
BVH3 RX1
                 61 TSHGDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
                                                                                  120
BVH3 JNR7/87
                 61 TSHGDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
                                                                                  120
BVH3 SP64
                 61 TSHGDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
                                                                                  120
                 61 TSHGDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
BVH3 P4241
                                                                                  120
BVH3 A66
                 61 TSHGDHYHYYNGKVPYDALFSEELLMKDPNYQLKDADIVNEVKGGYIIKVDGKYYVYLKD
                                                                                  120
BVH3 WU2
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
BVH3 RX1
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
                                                                                  180
BVH3 JNR7/87
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
                                                                                  180
BVH3 SP64
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
                                                                                  180
BVH3 P4241
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
                                                                                  180
BVH3 A66
               121 AAHADNVRTKDEINRQKQEHVKDNEKVNSNVAVARSQGRYTTNDGYVFNPADIIEDTGNA
                                                                                  180
BVH3 WU2
               181 YIVPHRGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTQSVAKGSTSK
                                                                                  240
BVH3 RX1
               181 YIVPHGGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTOSVAKGSTSK
                                                                                  240
BVH3 JNR7/87
               181 YIVPHGGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTQSVAKGSTSK
                                                                                  240
BVH3 SP64
               181 YIVPHGGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTOSVAKGSTSK
                                                                                  240
BVH3 P4241
               181 YIVPHRGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTQSVAKGSTSK
                                                                                  240
BVH3 A66
               181 YIVPHRGHYHYIPKSDLSASELAAAKAHLAGKNMQPSQLSYSSTASDNNTQSVAKGSTSK
BVH3 WU2
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHFIPYSK
                                                                                  300
BVH3 RX1
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHFIPYSK
                                                                                  300
BVH3 JNR7/87
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHPIPYSK
                                                                                  300
BVH3 SP64
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHFIPYSK
                                                                                  300
BVH3 P4241
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHFIPYSK
                                                                                  300
BVH3 A66
               241 PANKSENLQSLLKELYDSPSAQRYSESDGLVFDPAKIISRTPNGVAIPHGDHYHFIPYSK
                                                                                  300
                      BVH3 WU2
               301 LSALBEKIARMVPISGTGSTVSTNAKPNEVVSSLGSLSSNPSSLTTSKELSSASDGYIPN
                                                                                  360
BVH3 RX1
               301 LSALEEKIARRVPISGTGSTVSTNAKPNEVVSSLGSLSSNPSSLTTSKELSSASDGYIFN
                                                                                  360
BVH3 JNR7/87
               301 LSALBEKIARMVPISGTGSTVSTNAKPNEVVSSLGSLSSNFSSLTTSKELSSASDGYIFN
                                                                                  360
               301 LSALBEKIARMVPISGTGSTVSTNAKPNEVVSSLGSLSSNFSSLTTSKELSSASDGYIPN
BVH3 SP64
                                                                                  360
               301 LSALBEKIARMVPISGTGSTVSTNAKPNEVVSSLGSLSSNPSSLTTSKELSSASDGYIFN
BVH3 P4241
                                                                                  360
BVH3 A66
               301 LSALEEKIARMVPISGTGSTVSTNAKPNEVVSSLGSLSSNPSSLTTSKELSSASDGYIFN
                                                                                  360
BVH3 WU2
              361 PKDIVEETATAYIVRHGDHFHYIPKSNQIGQPTLPMNSLATPSPSLPINPGTSHEKHEED
                                                                                  420
BVH3 RX1
               361 PKDIVEETATAYIVRHGDHFHYIPKSNQIGQPTLPNNSLATPSPSLPINPGISHEKHEBD
                                                                                  420
BVH3 JNR7/87
               361 PKDIVEETATAYIVRHGDHFHYIPKSNQIGQPTLPNNSLATPSPSLPINPGTSHEKHEED
                                                                                  420
BVH3 SP64
               361 PKDIVEETATAYIVRHGDHFHYIPKSNQIGQPTLPNNSLATPSPSLPINPGTSHEKHEBD
                                                                                  420
BVH3 P4241
               361 PKDIVBETATAYIVRHGDHFHYIPKSNQIGQPTLPNNSLATPSPSLPINPGTSHEKHEED
                                                                                  420
BVH3 A.66
               361 PKDIVEETATAYIVRHGDHFHYIPKSNQIGQPTLPNNSLATPSPSLPINPGTSHEKHEED
                                                                                  420
BVH3 WU2
               421 GYGFDANRIIAEDESGFVMSHGDHNHYFFKKDLTEEQIKAAQKHLBEVKTSHNGLDSLSS
BVH3 RX1
               421 GYGFDANRIIAEDESGFIMSHGNHNHYFPKKDLTEEQIKAAQKHLEEVKTSHNGLDSLSS
BVH3 JNR7/87
               421 GYGFDANRIIAEDESGFVMSHGDHNHYFFKKDLTEEQIKAAQKHLEEVKTSHNGLDSLSS
                                                                                  480
BVH3 SP64
               421 GYGFDANRIIAEDESGFVMSHGDHNHYFFKKDLTEEQIKAAQKHLBEVKTSHNGLDSLSS
                                                                                  480
BVH3 P4241
               421 GYGFDANRIIAEDESGFVMSHGDHNHYFFKKDLTEEQIKAAQKHLEEVKTSHNGLDSLSS
                                                                                  480
BVH3 A66
               421 GYGFDANRIIAEDESGFVMSHGDHNHYFFKKDLTEEQIKAAQKHLEEVKTSHNGLDSLSS
                                                                                  480
```

```
BVH3 WU2
                481 HEQDYPSNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHHADPID
 BVH3 RX1
                 481 HEQDYPGNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHHADPID
 BVH3 JNR7/87
                481 HEQDYPSNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHHADPID
                                                                                   540
 BVH3 SP64
                481 HEQDYPGNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHHADPID
                                                                                   540
 BVH3 P4241
                481 HEQDYPSNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHHADPID
                                                                                   540
 BVH3 A66
                481 HEQDYPSNAKEMKDLDKKIEEKIAGIMKQYGVKRESIVVNKEKNAIIYPHGDHHKADPID
 BVH3 WU2
                541 EHKPVGIGHSHSNYELFKPBEGVAKKEGNKVYTGEBLTNVVNLLKNSTFNNQNFTLANGQ
                                                                                   600
                541 EHKPVGIGHSHSNYELFKPEEGVAKKEGNKVYTGEELTNVVNLLKNSTFNNQNFTLANGQ
 BVH3 RX1
                                                                                   600
                541 EHKPVGIGHSHSNYELFKPEEGVAKKEGNKVYTGEELTNVVNLLKNSTFNNQNFTLANGQ
 BVH3 JNR7/87
                                                                                   600
 BVH3 SP64
                541 EHKPVGIGHSHSNYELFKPBEGVAKKEGNKVYTGEELTNVVNLLKNSTFNNQNFTLANGQ
                                                                                   600
 BVH3 P4241
                541 EHKPVGIGHSHSNYELFKPEEGVAKKEGNKVYTGEELTNVVNLLKNSTFNNQNFTLANGQ
                                                                                   600
 BVH3 A66
                541 EHKPVGIGHSHSNYELFKPEEGVAKKEGNKVYTGEELTNVVNLLKNSTFNNQNFTLANGQ
                                                                                   600
 BVH3 WU2
                601 KRVSFSFPPELEKKLGINMLVKLITPDGKVLEKVSGKVFGEGVGNIANFELDQPYLPGOT
                                                                                   660
 BVH3 RX1
                601 KRVSFSPPPRLEKKLGINMLVKLITPDGKVLEKVSGKVPGRGVGNIANFELDQPYLPGQT
 BVH3 JNR7/87
                601 KRVSFSPPPBLEKKLGINMLVKLITPDGKVLEKVSGKVFGEGVGNIANFELDQPYLPGQT
 BVH3 SP64
                601 KRYSFSFPPELEKKLGINMLVKLITPDGKVLEKVSGKVFGEGVGNIANFBLDQPYLPGQT
                                                                                   660
 BVH3 P4241
                601 KRVSFSPPPELEKKLGINMLVKLITPDGKVLEKVSGKVFGEGVGNIANFELDQPYLPGQT
                                                                                   660
 BVH3 A66
                601 KRVSFSFPPELEKKLGINMLVKLITPDGKVLEKVSGKVFGEGVGNIANFELDQPYLPGQT
                                                                                   660
BVH3 WU2
                661 FKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPPHAGDTYLRVNPQFAVPKGTDAL
                                                                                   720
                661 PKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPPHAGDTYLRVNPQFAVPKGTDAL
 BVH3 RX1
                                                                                   720
                661 FKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPFHAGDTYLRVNPQFAVPKGTDAL
BVH3 JNR7/87
                                                                                   720
BVH3 SP64
                661 FKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPFHAGDTYLRVNPQPAVPKGTDAL
                                                                                   720
                661 FKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPFHAGDTYLRVNPQFAVPKGTDAL
BVH3 P4241
                                                                                   720
BVH3 A66
                661 FKYTIASKDYPEVSYDGTFTVPTSLAYKMASQTIFYPFHAGDTYLRVNPQFAVPKGTDAL
                                                                                   720
BVH3 WU2
                721 VRVFDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVH3 RX1
                721 VRVFDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVH3 JNR7/87
                721 VRVPDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVH3 SP64
                721 VRVFDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVH3 P4241
                721 VRVFDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVK3 A66
                721 VRVFDEFHGNAYLENNYKVGEIKLPIPKLNQGTTRTAGNKIPVTFMANAYLDNQSTYIVE
                                                                                   780
BVH3 WU2
                781 VPILEKENOTOKPSILPOPKRNKAQENSKFDEKVEEPKTSEKVEKEKLSETGNSTSNSTL
                                                                                  840
BVH3 RX1
                781 VPILEKENGTDKPSILPQFKRNKAQENSKLDEKVEEPKTSEKVEKEKLSETGNSTSNSTL
                                                                                   840
BVH3 JNR7/87
               781 VPILEKENQTDKPSILPQPKRNKAQENLKLDEKVEBPKTSEKVEKEKLSETGNSTSNSTL
                                                                                  840
BVH3 SP64
               781 VPILEKENGTDKPSILPQFKRNKAQENSKLDEKVERPKTSEKVEKEKLSETGNSTSNSTL
                                                                                  840
BVH3 P4241
               781 VPILEKENOTOKPSILPOPKRNKAQENSKPDEKVEEPKTSEKVEKEKLSETGNSTSNSTL
                                                                                  840
BVH3 A66
               781 VPILEKENQTOKPSILPQFKRNKAQENSKFDEKVEEPKTSEKVEKEKLSETGNSTSNSTL
                                                                                  840
BVH3 WU2
               841 EEVPTVDPVQEKVAKFAESYGMKLENVLPNMDGTIELYLPSGEVIKKNMADFTGEAPQGN
                                                                                  900
BVH3 RX1
               841 EEVPTVDPVQEKVAKFABSYGMKLENVLFNMDGTIELYLPSGEVIKKNMADFTGRAPOGN
                                                                                  900
BVH3 JNR7/87
               841 EEVPTVDPVQEKVAKFABSYGMKLENVLFNMDGTIBLYLPSGEVIKKNMADFTGEAPQGN
                                                                                  900
BVH3 SP64
               841 EEVPTVDPVQEKVAKFAESYGMKLENVLFNMDGTIELYLPSGEVIKKNMADFTGEAPQGN
                                                                                  900
BVH3 P4241
               841 EEVPTVDPVQEKVAKFAESYGMKLENVLFNMDGTIELYLPSGEVIKKNMADFTGEAPQGN
                                                                                  900
BVH3 A66
               841 EEVPTVDPVQEKVAKFAESYGMKLENVLFNMDGTIELYLPSGEVIKKNMADFTGEAPQGN
                                                                                  900
BVH3 WU2
               901 GENKPSENGKVSTGTVENQPTENKPADSLPEAPNEKPVKPENSTDNGMLNPEGNVGSDPM
BVH3 RX1
               901 GENKPSENGKVSTGTVENQPTENKPADSLPEAPNEKPVKPENSTDNGMLNPEGNVGSDPM
BVH3 JNR7/87
               901 GENKPSENGKVSTGTVENQPTENKPADSLPEAPNEKPVKPENSTDNGMLNPEGNVGSDPM
                                                                                  960
BVH3 SP64
               901 GENKPSENGKVSTGTVENQPTENKPADSLPEAPNEKPVKPENSTDNGMLNPEGNVGSDPM
                                                                                  960
BVH3 P4241
               901 GENKPSENGKVSTGTVENQPTENKPADSLPBAPNEKPVKPENSTDNGMLNP8GNVGSDPM
                                                                                  960
BVH3 A66
               901 GENKPSENGKVSTGTVENQPTENKPADSLPEAPNEKPVKPENSTDNGMLNPEGNVGSDPM
               961 LDPALEEAPAVDPVQEKLEKFTASYGLGLDSVIFMMDGTIELRLPSGEVIKKNLSDLIA 1019
BVH3 WU2
BVH3 RX1
               961 LDPALEEAPAVDPVQEKLEKPTASYGLGLDSVIFMMDGTIELRLPSGEVIKKNLSDLIA 1019
BVH3 JNR7/87
               961 LDPALEEAPAVDPVQEKLEKFTASYGLGLDSVIFMMDGTIELRLPSGEVIKKNLSDLIA 1019
BVH3 SP64
               961 LDPALBEAPAVDPVQEKLEKFTASYGLGLDSVIFNMDGTIELRLPSGEVIKKNLSDFIA 1019
BVH3 P4241
               961 LDPALEBAPAVDPVQEKLEKFTASYGLGLDSVIFNMDGTIBLRLPSGBVIKKNLSDLIA 1019
BVH3 A66
               961 LDPALEBAPAVDPVQEKLEKPTASYGLGLDSVIFNMDGTIELRLPSGEVIKKNLSDLIA 1019
```

FIGURE 11

```
BVH11-2 SP64
                     1 CSYELGRHQAGQVKKESNRVSYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDOGY
                                                                                      60
   BVH11-2 JNR7/87
                     1 CSYBLGRHQAGQVKKESNRVSYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDOGY
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11-2 P4241
   BVH11-2 A66
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11-2 WU2
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11-2 Rx1
                     1 CSYELGRHQAGQVKKESNRVSYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11 P4241
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEOIVIKITDOGY
   BVH11 WU2
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11 A66
   BVH11 Rx1
                     1 CSYELGRHQAGQVKKESNRVSYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
   BVH11 JNR7/87
                     1 CSYELGRHQAGQDKKESNRVAYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
                                                                                      60
   BVH11 SP63
                     1 CSYELGRHQAGQVKKESNRVSYIDGDQAGQKAENLTPDEVSKREGINAEQIVIKITDQGY
                                                                                      60
   BVH11 SP64
                     1 CAYELGLHQA-QTVKENNRVSYIDGKQATQKTENLTPDEVSKREGINAEQIVIKITDOGY
   BVH11-2 SP64
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVDGKYYVYLK 120
   BVH11-2 JNR7/87
                    61 VTSHGDHYHYYNGKVPYDAIISEBLLMKDPNYQLKDSDIVNEIKGGYVIKVDGKYYVYLK 120
   BVH11-2 P4241
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 120
   BVH11-2 A66
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 120
   BVH11-2 WU2
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNBIKGGYVIKVNGKYYVYLK 120
   BVH11-2 Rx1
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVDGKYYVYLK 120
   BVH11 P4241
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 120
   BVH11 WU2
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYGYLK 120
   BVH11 A.66
                    61 VTSHCDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 120
   BVH11 Fx1
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVDGKYYVYLK 120
   BVH11 JNR7/87
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 120
                    61 VTSHGDHYHYYNGKVPYDAIISEELLMKDPNYQLKDSDIVNEIKGGYVIKVDGKYYVYLK 120
   BVH11 SP63
                    60 VTSHGDHYHYYNGKVPYDAIISEBLLMKDPNYQLKDSDIVNEIKGGYVIKVNGKYYVYLK 119
   BVH11 SP64
   BVH11-2 SP64
                   121 DAAHADNIRTKEEIKRQKQEHSHNHNSRA---DNAVAAARAQGRYTTDDGYIFNASDIIE 177
   BVH11-2 JNR7/87 121 DAAHADNIRTKEEIKRQKQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
   BVH11-2 P4241
                   121 DAAHADNIRTKEEIKRQKQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
   BVH11-2 A66
                   121 DAAHADNIRTKEEIKRQRQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
   BVH11-2 WU2
                   121 DAAHADNIRTKEEIKRQKQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
   BVH11-2 Rx1
                   121 DAAHADNIRTKEEIKROKQERSHNHNSRA---DNAVAAARAQGRYTTDDGYIFNASDIIE 177
   BVH11 P4241
                   121 DAAHADNIRTKEEIKROKOEHSHNHGGGSN--DOAVVAARAOGRYTTDDGYIFNASDIIE 178
   BVH11 WU2
                   121 DAAHADNIRTKEEIKRQKQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
                   121 DAAHADNIRTKEEIKRQKQEHSHNHGGGSN--DQAVVAARAQGRYTTDDGYIFNASDIIE 178
   BVH11 A66
   BVH11 Rx1
                   121 DAAHADNIRTKEEIKRQKQERSHNHNSRA---DNAVAAARAQGRYTTDDGYIFNASDIIE 177
   BVH11 JNR7/87
                   121 DAAHADNIRTKEEIKRQKQERSHNHNSRA---DNAVAAARAQGRYTTDDGYIFNASDIIE 177
   BVH11 SP63
                   121 DAAHADNIRTKEEIKRQKQERSHNHNSRA---DNAVAAARAQGRYTTDDGYIFNASDIIE 177
   BVH11 SP64
                   120 DAAHADNVRTKEEINRQKQEHSQHREGGTSANDGAVAFARSQGRYTTDDGYIFNASDIIE 179
BVH11-2 SP64 178 DTGDAYIVPHGDHYHYIPKNELSASELAAAEAYWNGKQGSRPSSSSSYNANPVQPRLSEN 237
   BVH11-2 JNR7/87 179 DTGDAYIVPHGDHYHYIPKNELSASELAAAEAYWNGKQGSRPSSSSSYNANPAQPRLSEN 238
   BVH11-2 P4241 179 DTGDAYIVPHGNHFHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 238
                   179 DTGDAYIVPHGNHFHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 238
   BVH11-2 A66
   BVH11-2 WU2
                   179 DTGDAYIVPRGNHFHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSHNANPAQPRLSEN 238
   BVH11-2 Rx1
                   178 DTGDAYIVPHGDHYHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 237
   BVH11 P4241
                   179 DTGDAYIVPHGNHFHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 238
   BVH11 WU2
                   179 DTGDAYIVPHGNHFHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 238
   BVH11 A66
                   179 DTGDAYIVPHGNHPHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 238
   BVH11 Rx1
                   178 DTGDAYIVPHGDHYHYIPKSDLSASELAAAQAYWNGKQGSRPSSSSSHNANPAQPRLSEN 237
   BVH11 JNR7/87
                   178 DTGDAYIVPHGDHYHYIPKNELSASBLAAAEAYWNGKQGSRPSSSSYNANPAQPRLSEN 237
   BVH11 SP63
                   178 DTGDAYIVPHGNHFHYIPKSDLSASELAAAQAYWNGKOGSRPSSSSSHNANPAOPRLSEN 237
                   180 DTGDAYIVPHGDHYHYIPKNELSASELAAAEAFLSGRENLSNLRTYRRQNSDNTPRTNWV 239
   BVH11 SP64
                                   *.**** .*******.*. *...
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BVH11-2 SP64
                      238 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 285
      BVH11-2 JNR7/87 239 HNLTVTPTYHQN-------QGENISSLLRELYAKPLSERHVESDGLIFDPAOITS 286
                     239 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 286
      BVH11-2 P4241
                      239 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 286
      BVH11-2 A66
                     BVH11 - 2 WU2
      BVH11-2 Rx1
                      239 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 286
      BVH11 P4241
                      239 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 286
      BVH11 WU2
                      239 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 286
      BVH11 A66
                      238 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 285
      BVH11 Rx1
      BVH11 JNR7/87
                     238 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 285
      BVH11 SP63
                      238 HNLTVTPTYHQN------QGENISSLLRELYAKPLSERHVESDGLIFDPAQITS 285
      BVH11 SP64
                     240 PSVSNPGTTNTNTSNNSNTNSQASQSNDIDSLLKQLYKLPLSQRHVESDGLIFDPAQITS 299
                                                    * ***, .** ***, *, ********
      BVH11-2 SP64
                     286 RTARGVAVPHGNHYHFIPYEQMSELEKRIARIIPLRYRSNHWVPDSRPEQPSPQSTPEPS 345
      BVH11-2 JNR7/87 287 RTARGVAVPHGNHYHFIPYEQMSELEKRIARIIPLRYRSNHWVPDSRPEQPSPQSTPEPS 346
      BVH11-2 P4241
                     287 RTARGVAVPHGNHYHFIPYEQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQ----PS 342
      BVH11-2 A66
                      287 RTARGVAVPHGNHYHFIPYEQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQ----PS 342
      BVH11-2 WU2
                     287 RTARGVAVPHGNHYHFIPYEOMSELEERIARIIPLRYRSNHWVPDSRPEOPSPO----PS 342
      BVH11-2 Rx1
                     286 RTANGVAVPHGDHYHFIPYSQLSPLEEKLARIIPLRYRSNHWVPDSRPEQPSPQSTPEPS 345
      BVH11 P4241
                     287 RTARGVAVPHGNHYHFIPYEQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQ----PS 342
      BVH11 WU2
                     287 RTARGVAVPHGNHYHFIPYEQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQ----PS 342
      BVH11 A66
                     287 RTARGVAVPHGNHYHPIPYEQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQ----PS 342
      BVH11 Rx1
                      286 RTANGVAVPHGDHYHFIPYSQLSPLEEKLARIIPLRYRSNHWVPDSRPEQPSPQSTPEPS 345
      BVH11 JNR7/87
                     286 RTARGVAVPHGNHYHFIPYEQMSELEKRIARIIPLRYRSNHWVPDSRPEEPSPQPTPEPS 345
      BVH11 SP63
                     286 RTARGVAVPHGNHYHFIPYSQMSELEERIARIIPLRYRSNHWVPDSRPEQPSPQSTPEPS 345
      BVH11 SP64
                     300 RTARGVAVPHGNHYHFIPYEQMSELEKRIARIIPLRYRSNHWVPDSRPEEPSPOPTPEPS 359
      BVH11-2 SP64
                     346 PSLQPAPNPQPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 405
      BVH11-2 JNR7/87 347 PSPQPAPNPOPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSABTAAGIDSK 406
      BVH11-2 P4241
                     343 PSPQPAPNPQPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11-2 A66
                     343 PSPQPAPNPQPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11-2 WU2
                     343 PSPQPAPNPQPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11-2 Rx1
                     346 PSPQPAPNPQPAPSNPIDEKLVKRAVRKVGDGYVFEENGVPRYIPAKDLSAETAAGIDSK 405
      BVH11 P4241
                     343 PSPQPAPNPQPAPSNPIDEKLVKEAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11 WU2
                     343 PSPQPAPNPQPAPSNPIDEKLVKRAVRKVQDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11 A66
                     343 PSPQPAPNPQPAPSNPIDEKLVKBAVRKVGDGYVFEENGVSRYIPAKDLSAETAAGIDSK 402
      BVH11 Rx1
                     346 PSPQPAPNPQPAPSNPIDEKLVKBAVRKVGDGYVPEENGVPRYIPAKDLSAETAAGIDSK 405
                     346 PSP-----QPAPSNPIDEKLVKEAVRKVGDGYVPEENGVSRYIPAKDLSAETAAGIDSK 399
      BVH11 JNR7/87
      BVH11 SP63
                     346 PSPQSAPNPQPAPSNPIDEKLVKEVVRKVGDGYVFEKNGVSRYIPAKNLSAETAAGIDSK 405
      BVH11 SP64
                     360 PSPQPAPNPQPAPSNPIDEKLVKBAVRKVGDGYVPEENGVSRYIPAKNLSAETAAGIDSK 419
                              **********
      BVH11-2 SP64
                     406 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEVLDNLLERL 465
      BVH11-2 JNR7/87 407 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 466
9VH11-2 P4241
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 462
      BVH11-2 A66
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 462
      BVH11-2 WU2
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 462
      BVH11-2 Rx1
                     406 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHODLLDNKGRQVDFEALDNLLERL 465
      BVH11 P4241
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHODLLDNKGRQVDFEALDNLLERL 462
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 462
      BVH11 WU2
                     403 LAKQESLSHKLGTKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 462
      BVH11 A66
      BVH11 Rx1
                     406 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDILARIHQDLLDNKGRQVDFEALDNLLERL 465
      BVH11 JNR7/87
                     400 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 459
      BVH11 SP63
                     406 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 465
      BVH11 SP64
                     420 LAKQESLSHKLGAKKTDLPSSDREFYNKAYDLLARIHQDLLDNKGRQVDFEALDNLLERL 479
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BVH11-2 SP64
               466 KDVSSDKVKLVDDILAFLAPIRHPERLGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 525
BVH11-2 JNR7/87 467 KDVPSDKVKLVDDILAPLAPIRHPERLGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 526
BVH11-2 P4241
               463 KDVSSDKVKLVEDILAFLAPIRHPERLGKPNSQITYTDDEIQVAKLAGKYTTEDGY1FDP 522
BVH11-2 A66
               463 KDVSSDKVKLVEDILAFLAPIRHPERIGKPNSQITYTDDEIQVAKLAGKYTTEDGYIFDP 522
BVH11-2 WU2
               463 KDVSSDKVKLVEDILAFLAPIRHPERLGKPNSQITYTDDEIQVAKLAGKYTTEDGYIFDP 522
BVH11-2 Rx1
               466 KDVSSDKVKLVDDILAFLAPIRHPERLGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 525
BVH11 P4241
               463 KDVSSDKVKLVEDILAFLAPIRHPERLGKPNSQITYTDDEIQVAKLAGKYTTEDGYIFDP 522
BVH11 WU2
               463 KDVSSDKVKLVEDILAFLAPIRHPERLGKPNSQITYTDDEIQVAKLAGKYTTEDGYIFDP 522
BVH11 A66
               463 KDVSSDKVKLVEDILAFLAPIRHPERLGKPNSQITYTDDEIQVAKLAGKYTTEDGYIFDP 522
BVH11 Rx1
               466 KDVSSDKVKLVDDILAFLAPIRHPERIGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 525
BVH11 JNR7/87
               460 KDVSSDKVKLVDDILAFLAPIRHPERLGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 519
BVH11 SP63
               466 EDVPSDKVKLVDDILAFLAPIRHPERLGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 525
               480 KDVSSDKVKLVDDILAFLAPIRHPERIGKPNAQITYTDDEIQVAKLAGKYTTEDGYIFDP 539
BVH11 SP64
                       ****** *************** *******
BVH11-2 SP64
               526 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 585
BVH11-2 JNR7/87 527 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 586
BVH11-2 P4241
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHRDSGNTEAK 582
BVH11-2 A66
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHODSGNTEAK 582
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 582
BVH11-2 WU2
BVH11-2 Rx1
               526 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 585
BVH11 P4241
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 582
BVH11 WU2
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGMTEAK 582
BVH11 A66
               523 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 582
BVH11 Rx1
               526 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 585
BVH11 JNR7/87
               520 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTRAK 579
BVH11 SP63
               526 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTBAK 585
BVH11 SP64
               540 RDITSDEGDAYVTPHMTHSHWIKKDSLSEAERAAAQAYAKEKGLTPPSTDHQDSGNTEAK 599
BVH11-2 SP64
               586 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 645
BVH11-2 JNR7/87 587 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 646
               583 GABAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 642
BVH11-2 P4241
               583 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 642
BVH11-2 A66
BVH11-2 WU2
               583 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 642
BVH11-2 Rx1
               586 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKPEWFDEGLYEAPK 645
BVH11 P4241
               583 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 642
BVH11 WU2
               583 GABAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKPEWFDEGLYBAPK 642
BVH11 A66
               583 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 642
BVH11 Rx1
               586 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKPEWPDBGLYEAPK 645
BVH11 JNR7/87
               580 GAEAIYNRVKAAKKVPLDRMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 639
BVH11 SP63
               586 GAEAIYNRVKAAKKVPLORMPYNLQYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 645
BVH11 SP64
               600 GAEAIYNRVKAAKKVPLDRMPYNLOYTVEVKNGSLIIPHYDHYHNIKFEWFDEGLYEAPK 659
BVH11-2 SP64
               646 GYSLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK------ADQDSK 690
BVH11-2 JNR7/87 647 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK-------VDQDSK 691
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK------ADQDSK 687
BVH11-2 P4241
BVH11-2 A66
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK------ADQDSK 687
BVH11-2 WU2
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRXNK------ADQDSK 687
BVH11-2 Rx1
               646 GYSLEDLLATVKYYVEHPNERPHSDNGFGNASDHVQRNKNGQADTNQTEKPNEEKPQTEK 705
BVH11 P4241
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRXNK-------ADQDSK 687
BVH11 WU2
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK------ADODSK 687
BVH11 A66
               643 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVRKNK------ADQDSK 687
BVH11 Rx1
               646 GYSLEDLLATVKYYVEHPNERPHSDNGFGNASDHVORNK------NGO 687
BVK11 JNR7/87
               640 GYSLEDLLATVKYYVEHPNERPHSDNGFGNASDHVORNK-----NGO 681
BVH11 SP63
               646 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVQRNK-----NGO 687
BVH11 SP64
               660 GYTLEDLLATVKYYVEHPNERPHSDNGFGNASDHVQRNK-----NGQ 701
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BVH11-2 SP64
                 691 PDEDKEHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETBEEAEDTTDEAEIPQV 750
 BVH11-2 JNR7/87 692 PDEDKEHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETEEEAEDTTDEARIPQV 751
 BVH11-2 P4241
                 688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETEEEAEDTTDEAEIPQV 747
 BVH11-2 A66
                 688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTBETEEEAEDTTDEAEIPQV 747
 BVH11-2 WU2
                 688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTBETEBEAEDTTDEAEIPQV 747
BVH11-2 Rx1
                 706 PEEDKEHDEVSEPTHPESDEKENHVGLNPSADNLYKPSTDTEETEEEAEDTTDEAEIPQV 765
                 688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETEEEAEDTTDEAEIPQV 747
BVH11 P4241
BVH11 WU2
                 688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETEEEAEDTTDEAEIPQV 747
BVH11 A66
                688 PDEDKGHDEVSEPTHPESDEKENHAGLNPSADNLYKPSTDTEETEEEAEDTTDEAEIPQV 747
BVH11 Rx1
                 688 ADTNOTEKPNEEKPOTEKPEEETPREEKPOSEKPESPKPTEEPEERSPEESPEESEEPOV 747
BVH11 JNR7/87
                682 ADTNOTEKPNEEKPOTEKPEETPREEKPOSEKPESPKPTEEPEESPEESPEESEEPOV 741
BVH11 SP63
                688 ADTNOTEKPSEEKPQTEKPEEETPREEKPQSEKPESP----KPTEEPEEESPEESEEPQV 743
                702 ADTNOTEKPSEEKPQTEKPEEETPRBEKPQSEKPESP----KPTEBPEEESPEESBEPQV 757
BVH11 SP64
BVH11-2 SP64
                751 ENSVINAKIADAEALLEKYTDPSIRONAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 810
BVH11-2 JNR7/87 752 ENSVINAKIADAEALLEKVTDPSIRONAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 811
BVH11-2 P4241
                748 EHSVINAKIADABALLEKVTDPSIRQNAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 807
                748 EHSVINAKIADABALLEKVTDPSIRQNAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 807
BVH11-2 A66
BVH11-2 WU2
                748 EHSVINAKIADAEALLEKVTDPSIRONAMETLTGLKSSLLLGTKONNTISAEVDSLLALL 807
BVH11-2 Rx1
                766 EYSVINAKIAEAEALLEKVTDSSIRQNAVETLTGLKSSLLLGTKDNNTISAEVDSLLALL 825
BVH11 P4241
                748 EHSVINAKIADAEALLEKVTDPSIRQNAMETLTGLKSSLLLGTKONNTISAEVDSLLALL 807
BVH11 WU2
                748 EHSVINAKIADAEALLEKVTDPSIRQNAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 807
BVH11 A66
                748 EHSVINAKIADAEALLEKUTDPSIRQNAMETLTGLKSSLLLGTKDNNTISAEVDSLLALL 807
BVH11 Rx1
                748 ETEKVKEKLREAEDLLGKIQNPIIKSNAKETLTGLKNNLLFGTQDNNTIMAEAEKLLALL 807
BVH11 JNR7/87
                742 ETEKVKEKLREAEDLLGKIONPIIKSNAKETLTGLKNNLLFGTQDNNTIMAEAEKLLALL 801
BVH11 SP63
                744 ETEKVEEKLREAEDLLGKIQDPIIKSNAKETLTGLKNNLLFGTQDNNTIMAEAEKLLALL 803
BVH11 SP64
                758 ETEKVEEKLREAEDLLGKIQDPIIKSNAKETLTGLKNNLLFGTQDNNTIMAEAEKLLALL 817
                                           * ** ****** ** ** **** ** . ****
BVH11-2 SP64
                811 KESQPAPIO 819
BVH11-2 JNR7/87 812 KESQPAPIQ 820
BVH11-2 P4241
                808 KKSQPAPIQ 816
BVH11-2 A66
                808 KKSQPAPIQ 816
BVH11-2 WU2
                808 KKSQPAPIQ 816
BVH11-2 Rx1
                826 KESQPAPIQ 834
BVH11 P4241
                808 KESK
                              811
BVH11 WU2
                808 KESK
                              811
BVH11 A66
                808 KESK
                              811
BVH11 Rx1
                808 KESK
                              811
BVH11 JNR7/87
                802 KESK
BVH11 SP63
                804 KESK
                              807
BVH11 SP64
                818 KESK
                              821
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DVUII 2	DVUIL 2 DVUIL	DV777.4	2									
7-111140	CDC2	10 V CT	1	BVH!!	BVHII-2 BVHII	BVHII	BVH11-2	BVHII	BVH11-2	BVHII	BVH11-2	
2010	1	JINK. 1/8/	JNK. //8/	WU2	l wuz	A66	A66	P4241	P4241	-K-1	Rx-1	
I 81%	%88 I	%88 I	I 82%	1 80%	1 80%	I 80%	%08 I	%08 I	1 80%	1 88%	1 9 10/	וותיום
S 86%	S 90%	S 91%	S 87%	S 85%	S 85%	S 85%	S 85%	%58 8	%5% S	5 01%	0/101	Pyds
	1 87%	1 87%	%86 I	%\$6 I	1 96%	195%	I 96%	195%	7,961	187%	7070	מותוחום
	S 90%	S 90%	S 98%	%96 S	S 97%			%96 S	%26 S	%06 S	2 95%	2-1111-C
	*	%96 I	%88 I	1 88%	%28 I	%88 I		%88 I	187%	70261	7,608,1	RVHII
		%96 S	S 91%	S 91%	%06 S	8 91%	%06 S	S 91%	S 90%	S 97%	\$ 60%	SP63
			%L8 I	187%			%98 I	1 87%	1 86%	1 96%	%88 I	BVHII
			%06	S 91%			S 90%	\$ 91%	%06 S	%96 S	%06 S	JNR.7/87
				%96 I	-			%96 I	%/6 I	1 87%	1 94%	BVH11-2
				S 97%			S 98%	S 97%	S 98%	%06 S	S 95%	JNR.7/87
							%86 I	%66 I	1 98%	187%	1 92%	BVH11
					S 98%	S 94%	%86 S	%66 S	%86 S	S 91%	S 94%	WU2
						%86 I	%66 I	%86 I	1 99%	1 86%	I 93%	BVH11-2
					——J	S 98%		S 98%	S 99%	S 90%	S 95%	WU2
							%66 I	100%	%66 I	I 87%	I 92%	BVHII
							%66 S		%66 S	S 91%	S 94%	A66
				*						%98 I	I 93%	BVH11-2
							لتت	S 99%	%66 S	S 90%	S 95%	A66
									I 99%	%28 I	1 92%	BVH11
		ב מבוללום	ŗ						S 99%	S 91%	S 94%	P4241
		FIGURE 13	<u> </u>							%98 I	1 93%	BVH11-2
										S 90%	S 95%	P4241
											191%	BVH11
											S 92%	Rx-1

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AATTCCTTGT CGGGTAAGTT CCGACCCGCA CGAAAGGCGT AATGATTTGG GCACTGTCTC	60
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AAAA MAAAAAAAAAAAAAAAAAAAAAAA	240
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THE PARTY OF THE P	420
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	540
The second secon	600
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	780
	840
	900
	·_ 960
TTAGAAGTGG AAGTGTGGCG ACACATGTAG COGACTATA ATTGAATAGA TATTCAATTT CCAAAGTAAC TGAGAATATG AAAGCGAACG GTTTTCTTAG ATTGAATAGA TATTCAATTT CCAAAGTAAC TGAGAATATG AAAGCGAACG GTTTTCTTAG ACATAGACTT GTACCCATGC	1020
CCAAAGTAAC TGAGAATATG AAAGCGAACG GTTTCTTAGG AGATACACCT GTACCCATGC TGAGTAGGTA TTACTCAGAG TTAAGTGACG ATAGCCTAGG AGATACACCT GTACCCATGC	1080
TGAGTAGGTA TTACTCAGAG TTAAGTGACG ANACCCTAG GGGGTTGCCC CCTGTGAGAT CGAACACAGA AGTTAAGCCC TAGAACGCCG GAACTAGTTG GGGGTTGCCC CCTTACAAGC	1140
	1200
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TATCACTACA TICCCAAAAG CGATTATCT GCTAGTGAT TATCACAGC TAGTGACAAT CTGGCTGGAA AAAATATGCA ACCGAGTCAG TTAAGCTATT CTTCAACAGC TAGTGACAAT CTGGCTGGAA AAAATATGCA ACCGAGTCAG TAAGCTAT CTAAAAATCTC	2580
CTGGCTGGAA AAAATATGCA ACCGAGTCAG IRAGCTAT CAAAATAAATC TGAAAATCTC AACACGCAAT CTGTAGCAAA AGGATCAACT AGCAAGCCAG CAAATAAATC TGAAAAATCTC	2640
CAGAGTETT TGAAGGAACT CTATGATICA CETAGTECAC CAAATGGAGT TGCGATTCCG	2700
GGCCTGGTCT TTGACCCTGC TAAGATTATC AGCONGCTTT CTGCTTTAGA AGAAAAGATT	2760
CATGGCGACC ATTACCACTT TATTCCTTAC AGCAAGCTT CTGCAAATGC AAAACCTAAT GCCAGAATGG TGCCTATCAG TGGAACTGGT TCTACAGTTT CTTCTTTAAC GACAAGTAAG	2820
GCCAGAATGG TGCCTATCAG TGGAACTGGT ACCARTCATT CTTCTTTAAC GACAAGTAAG	2880
GAAGTAGTGT CTAGTCTAGG CAGTCTTCA AGCAATCCTT GTTGAAGAAACG GAGCTCTCTT CAGCATCTGA TGGTTATATT TTTAATCCAA AAGATATCGT TGAAGAAACG	2940
GAGCTCTCTT CAGCATCTGA TGGTTATATT TITAATCCAT ACATTCCAAA ATCAAATCAA	3000
GCTACAGCTT ATATTGTAAG ACATGGTGAT CATTLCCATT ACTTCCATC TCTTCCAATC ATTGGGCAAC CGACTCTTCC AAACAATAGT CTAGCAACAC CTTCTCCATC TCTTCCAATC	3060
ATTGGGCAAC CGACTCTTCC AAACAATAGI CIAGCAACAC SICOLOGIA TGCTAATCGT AATCCAGGAA CTTCACATGA GAAACATGAA GAAGATGGAT ACGGATTTGA TGCTAATCGT AATCCAGGAA CCACAA TCATTATTTC	3120
AATCCAGGAA CTTCACATGA GAAACATGAA GAAGATGGAT MOODALAA TCATTATTTC ATTATCGCTG AAGATCAATC AGGTTTTGTC ATGAGTCACG AAAACATTT AGAGGAAGTT	3180
ATTATCGCTG AAGATCAATC AGGTTTTGTC ATGAGTCACG CAAAAACATTT AGAGGAAGTT TTCAAGAAGG ACTTGACAGA AGAGCAAATT AAGGCTGCGC AAAAACATTT AGAGGAAGTT TTCAAGAAGG ACTTGACAGA AGAGCAAATT ATGATCTCATG AACAGGATTA TCCAGGTAAT	3240
	3300
AAAACTAGTC ATAATGGATT AGATTCTTTG TCATCTCATO INTO CATTATGAAA GCCAAAGAAA TGAAAGATTT AGATAAAAAA ATCGAAGAAA AAATTGCTGG CATTATGAAA	3360
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CAATATGGTG	TCAAACGTGA	AAGTATTGTC	GTGAATAAAG	AAAAAAATGC	GATIATIAT	3480
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A A MAR A MORENTA	ATACTCCACA	AGAATTAACG	AATGTTGTTA	ATTIGLIAAA	MARIAGIACO	3600
	A A A A CHIMINET A C.	ጥርተከርተርስልሞ	GGTCAAAAAC	GCGTTTCTTT	INGITIECE	3660
	TWILLERA	አርርጥልጥር እልፐ	ATGCTAGTAA	AATTAATAAC	ACCAGATOGA	3720
	NOR A ROTTATIO	TCCTDAAGTA	TTTGGAGAAG	GAGTAGGGAA	INIIOCHAC	3780
	አምሮአ አርርጥጥ	ተሞካ አርር አርር IA	CAAACATTA	MOININGINI	COCITCION	3840
as man mada a	አ አርሞስ አርሞዋል	TGATGGTACA	TTTACAGTTC	CAACCICITI	MOCITACHAN	3900
GATTATCCAG	AAACGATTTT	CTATCCTTTC	CATGCAGGGG	ATACTTATTT	AAGAGTGAAC	3960
ATGGCCAGIC	CAGTGCCTAA	ACCAACTGAT	GCTTTAGTCA	GAGTGTTTGA	TGAATTTCAT	4020
CCTCAATTTG	ATTTAGAAAA	TANCTATA AA	GTTGGTGAAA	TCAAATTACC	GATTCCGAAA	4080
GGAAATGCTT	GAACAACCAG	IMMCINIAM	DTTAAAATTC	CTGTAACCTT	CATGGCAAAT	4140
TTAAACCAAG	ACAATCAATC	CACTTATATT	GTGGAAGTAC	CTATCTTGGA	AAAAGAAAAT	4200
GCTTATTTGG	ACAATCAATC	TOTACCACAA	TTTAAAAGGA	ATAAAGCACA	AGAAAACTCA	4260
CAAACTGATA	AAAAGGTAGA	TCIMCCACA	ACTAGTGAGA	AGGTAGAAAA	AGAAAAACTT	4320
AAACTIGATG	GGAATAGTAC	MD CENTRO	ACCTTAGAAG	AAGTTCCTAC	AGTGGATCCT	4380
TCTGAAACTG	GGAATAGTAC AAGTAGCAAA	TAGIAATICA	ACCTINGGGA	TGAAGCTAGA	AAATGTCTTG	4440
GTACAAGAAA	AAGTAGCAAA ACGGAACAAT	ATTIGCIGAA	TTA CCATCAC	CAGAAGTCAT	TAAAAAGAAT	4500
TTTAATATGG	ACGGAACAAT TTACAGGAGA	TGAATTATAT	CONNECTO	AAAATAAACC	ATCTGAAAAT	4560
ATGGCAGATT	TTACAGGAGA	AGCACCTCAA	CARCCANCAG	AAAATAAACC	AGCAGATTCT	4620
GGAAAAGTAT	CTACTGGAAC	AGTIGAGAAC	LAACCAACAG	ACTCAACGGA	TAATGGAATG	4680
TTACCAGAGG	CACCAAACGA	AAAACCTGTA	AAACCAGAAA	ACTOAGCATT	AGAGGAAGCT	4740
TTGAATCCAG	AAGGGAATGT	GGGGAGTGAC	CCIMICITAG	CACCTACTTA	CGGATTAGGC	4800
CCAGCAGTAG	ATCCTGTACA	AGAAAAATTA	GAAAAAIIIA	man da marco	AAGTGGAGAA	4860
TTAGATAGTG	TTATATTCAA	TATGGATGGA	ACGATTGAAT	TARGATIOCC	AAGTGGAGAA	4920
GTGATAAAAA	AGAATTTATC	TGATTTCATA	GCGTAAGGAA	TAGCAGTAGA	AAAAGTCTGA	4980
ATCAAAAATG	AAGTTCTCTC	AAAAGTTAGA	AATAAAACTC	A A A CACCACC	חרבידים ביים	5040
TTTATTATTA	AAAATATATA	TTTCTTGACA	TACAACTTAA	MANGAGGIGG	MINITIAGE	5048
AGTTAATT	(SEQ ID NO	: 11)				2110

					*********	60
CAGAGATCTT	AGTGAATCAA	ATATACTTAA	GAAAAGAGGA	AAGAATGAAA	ATCHAINAAA	120
		בצוויות ערו עיויירי	TTITITIAALSIASI	CIGIOCIENT	01810-11-2	180
		מדמממתהאא	ATTIGITIE	CIMIUMOUS	00.2	240
	Maronara	מיויים ויושים א ליחידים	DITTACTOR	CWAGCATOLL	00.0.00	300
		ከምጥአ ሮርርር ከጥሮ	DAGGTTATGT	GWCCICICA	001101111	360
	MI I MAGAGE BA		DTRECCATUAL	CHOIGNAGAG	CICCICI	•
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		باسلمان البالا لابلاب لابلا	ACH THARGES	TOCHOCTON	0000	480
		*********	AALAALA	INGILLAGE	CO + 0. 2 . 0	540
			THE ALLEIN	MCMOOOMCOC	*******	600
		ፈጥልጥርማር ልጥል 	TTATEGAAGA	TWCGGGCGUT	00011111111	660
		יין דיידי אין אין איז	ADDIAGON'S	GIIMICAGCI	1700011	720
		warrant and a control of the control	AAAATURUL	WWWITITUDOU	Meering	780
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		**************************************	AL AL TAACAG	ICMMOCUMOT	C1 E 2 1 C 2 1 C 2 C	900
	mamamma a a a	<u> </u>	AACTIGCCTTT	GWGICMMCGC	CHICINGRAL	960
		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	TCACAAGTCG	AACCGCCAGA	GOIGINGCIO	: 1020
		יין דיים מידידים איי	CTTATGAACA	WAIGICIGMA	* * * * * * * * * * * * * * * * * * * *	1080
		יאדערבידיאיי	GTTCAAACCA	TIGGGTWC	O117 7 CT E 1-1-1-	1140
		~~^ እ	AACCTAGTCC	WWGICCGCW	CC1CC1CC1	1200
		እንጥሶሶሽ አማጣር	ATGAGAAATT	GUILMMUUM	0010110010.	1260
		カー・ファンス アイス・ストー・ストー・ストー・ストー・ストー・ストー・ストー・ストー・ストー・スト	ATTRICACTOR	ICGITATOR	C-10000000	1320
	TODACA CO.	מראכוכר ביוייוני	ATAGCAAACI		0.0000	1380
		רו או המיניים אא א א	TTTTATCTAG	IGWICGWOW	T 2 4 24 500	1440
		* ለ	AAGAT CTAUT	TOWINGTOOG	00100110111	1500
		N N CHOMOTOMICS CO.	AAITGAU IL AA	GOVIGICA	7101010	1560
			TAGETHE LEGAL	ICGICALCOA	0121001111	1620
		ביוויים מים מים אים ב	THUMBLE	I CWWG I WG A A	10101	1680
		יויי ויני מידי מידיידיטיטיטי	TRATELLE	IGNINIANCO	110 r o	1740
		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ATAGCUALIG	GWIIMMANN	OUTUO:	1800
	*********	- ACCCACCCTT	DITTOLINADIA	GWWGGTTIG	MCCCCTCCT	1860
		בווים ותייה או אורים	DINAMANTIA	MOCHONOCA	WY C TITLE I TO	1920 1980
		י אוייים מיתיתיתים	ATT THE ATTACL.	TINCHA	O4 O	2040
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		וויים מיבות העודיתיים	CACCTAAGGG	GININCICI	01700111011-	2160
		ነ <i>ለ</i> መረረር እእር እጥር	LIBARCGRALU	ILLUGUALIUM	OWINGTOOM	2220
		מ תבו א א הישישים ו	DITAAAAATIGU	ICHAGGION	176-40 HIT	2280
		י אארייירים בא	CAGAAAACC	TOMOGRAGA	, Mccccara	2340
		• ************************************	· CTCCAAAACU	MACHOROGO		2400
			TITITALIAL ILLIA	MANGGILGE		2460
		ייידע אות אוא או	' AGGERATE CAME	INICAROLO	, ,,,,	2520
						2580
		ויעינבובויי איאוווו	' 'I'A A A I SI SALSANI	INVOINT	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	2640
TTCTAACTC	TAAAAACAG(3 ATAGGAGAA	GGGAAAACGA	L AAAAIGAGA	CAGAATGTGA	2647
GTTCTAG	(SED ID NO	: 12)				

GGGTCTTAAA	ACTCTGAATC	CTTTAGAGGC	AGACCCACAA	AATGACAAGA	CCTATTTAGA	6	0
AAATCTGGAA	GAAAATATGA	GTGTTCTAGC	AGAAGAATTA	AAGTGAGGAA	AGAATGAAAA	12	-
TCAATAAAA	ATATCTAGCA	GGTTCAGTGG	CAGTCCTTGC	CCTAAGTGTT	TGTTCCTATG	18	0
				TAATCGAGTT		24	0
ATGGTGATCA	GGCTGGTCAA	AAGGCAGAAA	ATTTGACACC	AGATGAAGTC	AGTAAGAGAG	30	0
				TCAAGGTTAT		36	0
ATGGAGACCA	TTATCATTAC	TATAATGGCA	AGGTTCCTTA	TGATGCCATC	ATCAGTGAAG	42	0
AACTTCTCAT	GAAAGATCCG	AATTATCAGT	TGAAGGATTC	AGACATTGTC	AATGAAATCA	48	0
AGGGTGGCTA	TGTGATTAAG	GTAGACGGAA	AATACTATGT	TTACCTTAAA	GATGCGGCCC	54	0
ATGCGGACAA	TATTCGGACA	AAAGAAGAGA	TTAAACGTCA	GAAGCAGGAA	CACAGTCATA	60	0
ATCATAACTC	AAGAGCAGAT	AATGCTGTTG	CTGCAGCCAG	AGCCCAAGGA	CGTTATACAA	66	0
CGGATGATGG	GTATATCTTC	AATGCATCTG	ATATCATTGA	GGACACGGGT	GATGCTTATA	72	0
TCGTTCCTCA	CGGCGACCAT	TACCATTACA	TTCCTAAGAA	TGAGTTATCA	GCTAGCGAGT	78	0
TAGCTGCTGC	AGAAGCCTAT	TGGAATGGGA	AGCAGGGATC	TCGTCCTTCT	TCAAGTTCTA	84	0
GTTATAATGC	AAATCCAGTT	CAACCAAGAT	TGTCAGAGAA	CCACAATCTG	ACTGTCACTC	90	0
CAACTTATCA	TCAAAATCAA	GGGGAAAACA	TTTCAAGCCT	TTTACGTGAA	TTGTATGCTA	96	0
AACCCTTATC	AGAACGCCAT	GTAGAATCTG	ATGGCCTTAT	TTTCGACCCA	GCGCAAATCA	102	0
CAAGTCGAAC	CGCCAGAGGT	GTAGCTGTCC	CTCATGGTAA	CCATTACCAC	TTTATCCCTT	108	0
TAAAAAT	GTCTGAATTG	GAAAAACGAA	TTGCTCGTAT	TATTCCCCTT	CGTTATCGTT	114	0
CAAACCATTG	GGTACCAGAT	TCAAGACCAG	AACAACCAAG	TCCACAATCG	ACTCCGGAAC	120	0
CTAGTCCAAG	TCTGCAACCT	GCACCAAATC	CTCAACCAGC	TCCAAGCAAT	CCAATTGATG	126	0
AGAAATTGGT	CAAAGAAGCT	GTTCGAAAAG	TAGGCGATGG	TTATGTCTTT	GAGGAGAATG	132	0
GAGTTTCTCG	TTATATCCCA	GCCAAGGATC	TTTCAGCAGA	AACAGCAGCA	GGCATTGATA	138	0
GCAAACTGGC	CAAGCAGGAA	AGTTTATCTC	ATAAGCTAGG	AGCTAAGAAA	ACTGACCTCC	144	0
CATCTAGTGA	TCGAGAATTT	TACAATAAGG	CTTATGACTT	ACTAGCAAGA	ATTCACCAAG	150	0
ATTTACTTGA	TAATAAAGGT	CGACAAGTTG	ATTTTGAGGT	TTTGGATAAC	CTGTTGGAAC	156	0
GACTCAAGGA	TGTCTCAAGT	GATAAAGTCA	AGTTAGTGGA	TGATATTCTT	GCCTTCTTAG	162	0
CTCCGATTCG	TCATCCAGAA	CGTTTAGGAA	AACCAAATGC	GCAAATTACC	TACACTGATG	168	0
ATGAGATTCA	AGTAGCCAAG	TTGGCAGGCA	AGTACACAAC	AGAAGACGGT	TATATCTTTG	174	0
ATCCTCGTGA	TATAACCAGT	GATGAGGGGG	ATGCCTATGT	AACTCCACAT	ATGACCCATA	180	0
GCCACTGGAT	TAAAAAAGAT	AGTTTGTCTG	AAGCTGAGAG	AGCGGCAGCC	CAGGCTTATG	186	0
CTAAAGAGAA	AGGTTTGACC	CCTCCTTCGA	CAGACCACCA	GGATTCAGGA	AATACTGAGG	192	0
CAAAAGGAGC	AGAAGCTATC	TACAACCGCG	TGAAAGCAGC	TAAGAAGGTG	CCACTIGATC	198	0
GTATGCCTTA	CAATCTTCAA	TATACTGTAG	AAGTCAAAAA	CGGTAGTTTA	ATCATACCTC	204	0
ATTATGACCA	TTACCATAAC	ATCAAATTTG	AGTGGTTTGA	CGAAGGCCTT	TATGAGGCAC	210	0
CTAAGGGGTA	TAGTCTTGAG	GATCTTTTGG	CGACTGTCAA	GTACTATGTC	GAACATCCAA	216	0
ACGAACGTCC	GCATTCAGAT	AATGGTTTTG	GTAACGCTAG	TGACCATGTT	CGTAAAAATA	222	0
AGGCAGACCA	AGATAGTAAA	CCTGATGAAG	ATAAGGAACA	TGATGAAGTA	AGTGAGCCAA	228	0.
CTCACCCTGA	ATCTGATGAA	AAAGAGAATC	ACGCTGGTTT	AAATCCTTCA	GCAGATAATC	234	-
TTTATAAACC	AAGCACTGAT	ACGGAAGAGA	CAGAGGAAGA	AGCTGAAGAT	ACCACAGATG	240	-
AGGCTGAAAT	TCCTCAAGTA	GAGAATTCTG	TTATTAACGC	TAAGATAGCA	GATGCGGAGG	246	
CCTTGCTAGA	AAAAGTAACA	GATCCTAGTA	TTAGACAAAA	TGCTATGGAG	ACATTGACTG	252	
GTCTAAAAAG	TAGTCTTCTT	CTCGGAACGA	AAGATAATAA	CACTATTTCA	GCAGAAGTAG	258	_
ATAGTCTCTT	GGCTTTGTTA	AAAGAAAGTC	AACCGGCTCC	TATACAGTAG	TAAAATGAA	263	9
(SEQ ID NO	: 13)						

MKINKKYLAG	SVAVLALSVC	SYELGRHQAG	QVKKESNRVS	YIDGDQAGQK	50
AENLTPDEVS	KREGINAEQI	VIKITDQGYV	TSHGDHYHYY	NGKVPYDAII	100
SEELLMKDPN	YQLKDSDIVN	EIKGGYVIKV	DGKYYVYLKD	AAHADNIRTK	150
EEIKRQKQEH	SHNHNSRADN	AVAAARAQGR	YTTDDGYIFN	ASDITEDTGD	200
AYIVPHGDHY	HYIPKNELSA	SELAAABAYW	NGKQGSRPSS	SSSYNANPVQ	250
PRLSENHNLT	VTPTYHQNQG	ENISSLLREL	YAKPLSERHV	ESDGLIFDPA	300
OITSRTARGV	AVPHGNHYHF	IPYEOMSELE	KRIARIIPLR	YRSNHWVPDS	350
RPEOPSPOST	PEPSPSLOPA	PNPQPAPSNP	IDEKLVKEAV	RKVGDGYVFE	400
ENGVSRYIPA	KDLSAETAAG	IDSKLAKQES	LSHKLGAKKT	DLPSSDREFY	450
NKAYDLLARI	HODLLDNKGR	QVDFEVLDNL	LERLKDVSSD	KVKLVDDILA	500
FLAPIRHPER	LGKPNAQITY	TDDEIQVAKL	AGKYTTEDGY	IFDPRDITSD	550
EGDAYVTPHM			AYAKEKGLTP	PSTDHQDSGN	600
TEAKGAEAIY	NRVKAAKKVP	LDRMPYNLQY	TVEVKNGSLI	IPHYDHYHNI	650
KFEWFDEGLY	EAPKGYSLED	LLATVKYYVE	HPNERPHSDN	GFGNASDHVR	700
KNKADODSKP	DEDKEHDEVS	EPTHPESDEK	ENHAGLNPSA	DNLYKPSTDT	750
EETEEEAEDT	TDEAEIPOVE	NSVINAKIAD	AEALLEKVTD	PSIRQNAMET	800
LTGLKSSLLL	GTKDNNTISA	EVDSLLALLK	ESQPAPIQ		838
(SEQ ID NO	: 14)				
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		GCATCGTTCG				60
		AAGTCAGAAA				120
		TGAGCAAATT				180
		TCATTACTAT				240
		GGATCCAAAC				300
GAAGTCAAGG	GTGGTTATAT	CATCAAGGTC	GATGGAAAAT	ATTATGTCTA	CCTGAAAGAT	360
GCAGCTCATG	CTGATAATGT	TCGAACTAAA	GATGAAATCA	ATCGTCAAAA	ACAAGAACAT	420
GTCAAAGATA	ATGAGAAGGT	TAACTCTAAT	GTTGCTGTAG	CAAGGTCTCA	GGGACGATAT	480
		CTTTAATCCA				540
		TCACTATCAC				600
		ACATCTGGCT				660
TATTCTTCAA	CACCTTCTCC	ATCTCTTCCA	ATCAATCCAG	GAACTTCACA	TGAGAAACAT	720
GAAGAAGATG	GATACGGATT	TGATGCTAAT	CGTATTATCG	CTGAAGATGA	ATCAGGTTTT	780
GTCATGAGTC	ACGGAGACCA	CAATCATTAT	TTCTTCAAGA	AGGACTTGAC	AGAAGAGCAA	840
ATTAAGGCTG	CGCAAAAACA	TTTAGAGGAA	GTTAAAACTA	GTCATAATGG	ATTAGATTCT	900
TTGTCATCTC	ATGAACAGGA	TTATCCAAGT	AATGCCAAAG	AAATGAAAGA	TTTAGATAAA	960
		TGGCATTATG				1020
		TGCGATTATT				1080
CCGATTGATG	AACATAAACC	GGTTGGAATT	GGTCATTCTC	ACAGTAACTA	TGAACTGTTT	1140
		TAAAAAAGAA				1200
ACGAATGTTG	TTAATTTGTT	AAAAAATAGT	ACGTTTAATA	ATCAAAACTT	TACTCTAGCC	1260
		TTTTAGTTTT				1320
		AACACCAGAT				1380
		GAATATTGCA				1440
		TATCGCTTCA				1500
		TTTAGCTTAC				1560
		TTTAAGAGTG				1620
		TGATGAATTT				1680
		ACCGATTCCG				1740
		CTTCATGGCA				1800
		GGAAAAAGAA				1860
		ACAAGAAAAC				1920
AAGACTAGTG	AGAAGGTAGA	AAAAGAAAAA	CTTTCTGLAA	CTGGGAATAG	TACTAGTAAT	1980
		TACAGTGGAT				2040
		AGAAAATGTC				2100
TATTTACCAT	CGGGAGAAGT	CATTAAAAAG	AATATGGCAG	ATTTTACAGG	AGAAGCACCT	2160
CAAGGAAATG	GTGAAAATAA	ACCATCIGAA	AATGGAAAAG	TATCTACTGG	AACAGTTGAG	2220
AACCAACCAA	CAGAAAATAA	ACCAGCAGAT	TCTTTACCAG	AGGCACCAAA	CGAAAAACCT	2280
GTAAAACCAG	AAAACTCAAC	GGATAATGGA	ATGITGAATC	CAGAAGGGAA	TOTGGGGAGT	2340
GACCCTATGT	TAGATTCAGC	ATTAGAGGAA	COCTURACTAG	CTCTTATATATA	CARCHANAA	2400 2460
TTAGAAAAAT	TIACAGCTAG	TTACGGATTA GCCAAGTGGA	GUNGAGATAA	DIGITALATI	ATTCATCTCA	2520
	(SEO ID NO		GMAGIGMIAA	NAMADAATII	ATTOMICICA	2528
TAGCITAA	OBO ID NO	: T21				2,20



CAYALNOHRS	QENKDNNRVS	YVDGSQSSQK	SENLTPDQVS	QKEGIQAEQI	50
VIKITDQGYV	TSHGDHYHYY	NGKVPYDALF	SEELLMKDPN	YQLKDADIVN	100
EVKGGYIIKV	DGKYYVYLKD	AAHADNVRTK	DEINRQKQEH	VKDNEKVNSN	150
VAVARSQGRY	TTNDGYVFNP	ADIIEDTGNA	YIVPHGGHYH	YIPKSDLSAS	200
ELAAAKAHLA	GKNMQPSQLS	YSSTPSPSLP	INPGTSHEKH	EEDGYGFDAN	250
RIIAEDESGF	VMSHGDHNHY	FFKKDLTEEQ	IKAAQKHLEE	VKTSHNGLDS	300
LSSHEQDYPS	NAKEMKDLDK	KIEEKIAGIM	KQYGVKRESI	VVNKEKNAII	350
YPHGDHHHAD	PIDEHKPVGI	GHSHSNYELF	KPEEGVAKKE	GNKVYTGEEL	400
		NGQKRVSFSF			450
GKVLEKVSGK	VFGEGVGNIA	NFELDQPYLP	GQTFKYTIAS	KDYPEVSYDG	500
TFTVPTSLAY	KMASQTIFYP	FHAGDTYLRV	NPQFAVPKGT	DALVRVFDEF	550
HGNAYLENNY	KVGEIKLPIP	KLNQGTTRTA	GNKIPVTFMA	NAYLDNQSTY	600
IVEVPILEKE	NQTDKPSILP	QFKRNKAQEN	SKLDEKVEEP	KTSEKVEKEK	650
LSETGNSTSN	STLEEVPTVD	PVQEKVAKFA	ESYGMKLENV	LFNMDGTIEL	700
YLPSGEVIKK	NMADFTGEAP	QGNGENKPSE	NGKVSTGTVE	NQPTENKPAD	750
SLPEAPNEKP	VKPENSTDNG	MLNPEGNVGS	DPMLDSALEE	APAVDPVQEK	800
LEKFTASYGL	GLDSVIFNMD	GTIELRLPSG	EVIKKNLLIS		840
(SEC TO NO	. 16)			•	

CAYALNOHRS	QENKDNNRVS	YVDGSQSSQK	SENLTPDQVS	QKEGIQAEQI	50
VIKITDOGYV	TSHGDHYHYY	NGKVPYDALF	SEELLMKDPN	YQLKDADIVN	100
EVKGGYIIKV	DGKYYVYLKD	AAHADNVRTK	DEINRQKQEH	VKDNEKVNSN	150
VAVARSQGRY	TTNDGYVFNP	ADIIEDTGNA	YIVPHGGHYH	YIPKSDLSAS	200
ELAAAKAHLA	GKNMQPSQLS	YSSTASDNNT	QSVAKGSTSK	PANKSENLQS	250
LLKELYDSPS	AQRYSESDGL	VFDPAKIISR	TPNGVAIPHG	DHYHFIPYSK	300
LSALEEKIAR	MVPISGTGST	VSTNAKPNEV	VSSLGSLSSN	PSSLTTSKEL	350
SSASDGYIFN	PKDIVEETAT	AYIVRHGDHF	HYIPKSNQIG	QPTLPNNSLA	400
TPSPSLPINP	GTSHEKHEED	GYGFDANRII	AEDESGFVMS	HGDHNHYFFK	450
KDLTEEQIKA	AOKHLEEVKT	SHNGLDSLSS	HEODYPGNAK	EMKDLDKKIE-	500
EKIAGIMKOY	GVKRESIVVN	KEKNAIIYPH	GDHHHADPID	EHKPVGIGHS	550
HSNYELFKPE	EGVAKKEGNK	VYTGEELTNV	VNLLKNSTFN	NONFTLANGO	600
KRVSFSFPPE	LEKKLGINML	VKLITPDGKV	LEKVSGKVFG	EGVGNIANFE	650
LDQPYLPGOT	FKYTIASKDY	PEVSYDGTFT	VPTSLAYKMA	SOTIFYPFHA	700
GDTYLRVNPQ	FAVPKGTDAL	VRVFDEFHGN	AYLENNYKVG	EIKLPIPKLN	750
	IPVTFMANAY	LDNQSTYIVE		DKPSILPOFK	
RNKAQENSKL	DEKVEEPKTS		TONSTENSTL	EEVPTVDPVO	850
_	GMKLENVLFN		SGEVIKKNMA	DFTGEAPOGN	900
GENKPSENGK			EAPNEKPVKP	ENSTONGMLN	950
PEGNVGSDPM	LDPALEEAPA.			SVIFNMDGTI	1000
	KKNLSDFIA	(SEO ID NO		.,	1019
		, , , , , , , , , , , , , , , , , , , ,			

FIGURE 20

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CAYALNOHRS	OENKDNNRVS	YVDGSQSSQK	SENLTPDQVS	QKEGIQAEQI	50
VIKITDOGYV	TSHGDHYHYY	NGKVPYDALF	SEELLMKDPN	YQLKDADIVN	100
EVKGGYIIKV	DGKYYVYLKD	AAHADNVRTK	DEINRQKQEH	VKDNEKVNSN	150
VAVARSOGRY	TTNDGYVFNP	ADIIEDTGNA	YIVPHGGHYH	YIPKSDLSAS	200
ELAAAKAHLA	GKNMQPSQLS	YSSTASDNNT	QSVAKGSTSK	Panksenlos	250
LLKELYDSPS	AQRYSESDGL	VFDPAKIISR	TPNGVAIPHG	DHYHFIPYSK	300
LSALEEKIAR	MVPISGTGST	VSTNAKPNEV	VSSLGSLSSN	PSSLTTSKEL	350
SSASDGYIFN	PKDIVEETAT	AYIVRHGDHF	HYIPKSNQIG	QPTLPNNSLA	400
TPSPSLPINP	GTSHEKHEED	GYGFDANRII	AEDESGFVMS	HGDHNHYFFK	450
KDLTEEQIKA	AQKHLEEVKT	SHNGLDSLSS	HEQDYPGNA		. 489
(SEQ ID NO	: 56)				

MKFSKKYIAA GSAVIVSLSL C QKEGIQAEQI VIKITDQGYV T EVKGGYIIKV DGKYYVYLKD A	SHGDHYHYY AHADNVRTK	NGKVPYDALF DEINRQKQEH	VKDNEKVNSN	YQLKDADIVN VAVARSQGRY	180
TTNDGYVFNP ADIIEDTGNA Y YSSTASDNNT QSVAKGSTSK F TPNGVAIPHG DHYHFIPYSK I	VIVPHGGHYH PANKSENLQS LSALEEKIAR	YIPKSDLSAS LLKELYDSPS MVPISGTGST	ELAAAKAHLA AQRYSESDGL VSTNAKPNEV	GKNMQPSQLS VFDPAKIISR VSSLGSLSSN	300 360
PSSLTTSKEL SSASDGYIFN F TPSPSLPINP GTSHEKHEED G AQKHLEEVKT SHNGLDSLSS F	GYGFDANRII	AYIVRHGDHF AEDESGFVMS (SEQ ID NO	HGDHNHYFFK	KDLTEEQIKA	420 480 509

FIGURE 22

DLTEEQIKAA	OKHLEEVKTS	HNGLDSLSSH	EQDYPGNAKE	MKDLDKKIEE	50
KIAGIMKOYG	VKRESIVVNK	EKNAIIYPHG"	DHHHADPIDE	HKPVGIGHSH	100
SNYELFKPEE	GVAKKEGNKV	YTGEELTNVV	NLLKNSTFNN	QNFTLANGQK	150
RVSFSFPPEL	EKKLGINMLV	KLITPDGKVL	EKVSGKVFGE	GVGNIANFEL	200
DOPYLPGOTF	KYTIASKDYP	EVSYDGTFTV	PTSLAYKMAS	QTIFYPFHAG	250
DTYLRVNPQF	AVPKGTDALV	RVFDEFHGNA	YLENNYKVGE	IKLPIPKLNQ	300
GTTRTAGNKI	PVTFMANAYL	DNOSTYIVEV	PILEKENQTD	KPSILPQFKR	350
NKAOENSKLD	EKVEEPKTSE	KVEKEKLSET	GNSTSNSTLE	EVPTVDPVQE	400
KVAKFAESYG	MKLENVLFNM	DGTIELYLPS	GEVIKKNMAD	FTGEAPQGNG	450
ENKPSENGKV	STGTVENOPT	ENKPADSLPE	APNEKPVKPE	NSTDNGMLNP	500
EGNVGSDPML	DPALEEAPAV	DPVQEKLEKF	TASYGLGLDS	VIFNMDGTIE	550
LRLPSGEVIK	KNLSDFIAKL	RYRSNHWVPD	SRPEEPSPQP	TPEPSPSPQP	600
APNPOPAPSN	PIDEKLVKEA	VRKVGDGYVF	EENGVSRYIP	AKNLSAETAA	650
GIDSKLAKOE	SLSHKLGAKK	TDLPSSDREF	YNKAYDLLAR	IHQDLLDNKG	700
ROVDFEALDN	LLERLKOVSS	DKVKLVDDIL	AFLAPIRHPE	RLGKPNAQIT	750
YTDDEIQVAK	LAGKYTTEDG	YIFDPRDITS	DEGDAYVTPH	MTHSHWIKKD	800
SLSEAERAAA	QAYAKEKGLT	PPSTDHQDSG	NTEAKCAEAI	ynrvkaakkv	850
PLDRMPYNLQ	YTVEVKNGSL	IIPHYDHYHN	IKFEWFDEGL	YEAPKGYTLE	900
DLLATVKYYV	EHPNERPHSD	NGFGNASDHV	QRNKNGQADT	NQTEKPSEEK	950
POTEKPEEET	PREEKPQSEK	PESPKPTEEP	EEESPEESEE	PQVETEKVEE	1000
KLREAEDI.LG	KIQDPIIKSN	AKETLTGLKN	NLLFGTQDNN	TIMAEAEKLL	1050
	(SEQ ID NO	: 58)			1057

FIGURE 23

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04 FEBRUARY 2000. (04 CA 009901218 CAYALNOHRS QENKONNRVS YVDGSQSSQK SENLTPDQVS QKEGIQAEQI VIKITDQGYV TSHGDHYHYY NGKVPYDALF SEELLMKDPN YQLKDADIVN 100 EVKGGYIIKV DGKYYVYLKD AAHADNVRTK DEINRQKQEH VKDNEKVNSN 150 VAVARSQGRY TTNDGYVFNP ADIIEDTGNA YIVPHGGHYH YIPKSDLSAS 200 205 (SEQ ID NO : 59) FIGURE 24

	OWNERNDIDUC	YIDGKQATQK	TENLTPDEVS	KREGINAEQI	50
	QTVKENNRVS	NGKVPYDAII	SEELLMKDPN	YQLKDSDIVN	100
VIKITDQGYV				SOHREGGTSA	150
EIKGGYVIKV	NGKYYVYLKD			DHYHYIPKNE	200
NDGAVAFARS	QGRYTTDDGY	IFNASDIIED	TGDAYIVPHG		
	AFLSGRENLS	NLRTYRRQNS	DNTPRTNWVP	TUTTDANSAS	250
		LLKQLYKLPL	SQRHVESDGL	IFDPAQITSR	300
	QASQSNDIDS	MSELEKRIAR		WVPDSRPEEP	350
TARGVAVPHG	NHYHFIPYEQ			GYVFEENGVS	400
SPOPTPEPSP	SPQPAPNPQP	APSNPIDEKL			450
RYIPAKNLSA		AKQESLSHKL	GAKKTDLPSS		
		ALDNLLERLK	DVSSDKVKLV	DDILAFLAPI	500
LLARIHQDLL		OVAKLAGKYT	TEDGYIFDPR	DITSDEGDAY	550
RHPERLGKPN			KGLTPPSTDH		600
VTPHMTHSHW		RAAAQAYAKE		HYHNIKFEWF	650
AEAIYNRVKA	AKKVPLDRMP	YNLQYTVEVK	• • •		700
DEGLYEAPKG		KYYVEHPNER	PHSDNGFGNA		
		EEETPREEKP	QSEKPESPKP	TEEPBEESPE	750
QADTNQTEKP			IKSNAKETLT	GLKNNLLFGT	800
ESEEPQVETE	KVEEKLREAE		ID NO : 60)		821
QDNNTIMAEA	EKLLALLKES	K ((SEQ	12	25	
			L'TOUKE 5		

	YIDGKQATQK TENLTPDEVS KREGINAEQI	50
CAYELGLHQA QIVKENNRVS	NGKVPYDAII SEELLMKDPN YQLKDSDIVN	100
VIKITDQGYV TSHGDHYHYY	NGKVPIDATI SEENBOKOEH SOHREGGTSA	150
EIKGGYVIKV NGKYYVYLKD	AAHADNVRTK EEINRQKQEH SQHREGGTSA	200
NDGAVAFARS QGRYTTDDGY	IFNASDIIED TGDAYIVPHG DHYHYIPKNE	250
	MILDTORRONS UNITERINARY SASKESTANT	
ATTENNENTIS OASOSNOIDS	PPKOPAKTAT SOKMATSDOR TIPINGTION	334
TARGVAVPHG NHYHFIPYEQ	MSELEKRIAR IIPL	334
(SEQ ID NO : 61)	ETGIPE 26	4.5.5.5.5.5

TDLPSSDREF YNKAY DKVKLVDDIL AFLAP YIFDPRDITS DEGDA PPSTDHQDSG NTEAK IIPHYDHYHN IKFEW	SRYIP AKNLSAETAA DLLAR IHQDLLDNKG IRHPE RLGKPNAQIT YVTPH MTHSHWIKKD GAEAI YNRVKAAKKV IFDEGL YEAPKGYTLE IGQADT NQTEKPSEEK DEESEE POVETEKVEE	RQVDFEALDN YTDDEIQVAK SLSEAERAAA PLDRMPYNLQ DLLATVKYYV PQTEKPEEET KLREAEDLLG	LLERLKDVSS LAGKYTTEDG QAYAKEKGLT YTVEVKNGSL EHPNERPHSD PREEKPQSEK	50 100 150 200 250 300 350 400 450 487
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(SEQ ID NO : 62)

FIGURE 27

FIGURE 26

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.00	•	
AEAFLSGREN LSNLRTYRR	THENNETHTH TTDENEVERY WHITHTHEN C	50
	L PLSQRHVESD GLIFDPAQIT SRTARGVAVP	100
	I ARIIPLRYRS NHWVPDSRPE EPSPQPTPEP	150
	E KLVKEAVRKV GDGYVFEENG VSRYIPAKNL	200
SAETAAGIDS KLAKQESLS	H KLGAKKTOLP SSDREFYNKA YDLLARIHQD	250
LLDNKGRQVD FEALDNLLE	R LKDVSSDKVK LVDDILAFLA PIRHPERLGK	300
PNAQITYTDD EIQVAKLAG	K YTTEDGYIFD PRDITSDEGD AYVTPHMTHS	350
HWIKKDSLSE AERAAAQAY	A KEKGLTPPST DHQDSGNTEA KGAEAIYNRV	400
KAAKKVPLDR MPYNLQYTV	E VKNGSLIIPH YDHYHNIKFE WFDEGLYEAP	450
KGYTLEDLLA TVKYYVEHP	N ERPHSDNGFG NASDHVQRNK NGQADTNQTE	500
KPSEEKPQTE KPEEETPRE	E KPOSEKPESP KPTEEPEES PEESEEPOVE	550
TEKVEEKLRE AEDLLGKIQ	D PIIKSNAKET LTGLKNNLLF GTQDNNTIMA	600
	Q ID NO : 63)	613
	FIGURE 28	
	HNGLDSLSSH EQDYPGNAKE MKDLDKKIEE	50
KIAGIMKQYG VKRESIVVN	K EKNAIIYPHG DHHHADPIDE HKPVGIGHSH	100
	V YTGEELTHVV NLLKNSTFNN QNFTLANGQK	150
	V KLITPDGKVL EKVSGKVFGE GVGNIANFEL	200
	P EVSYDGTFTV PTSLAYKMAS QTIFYPFHAG	250
	/ RVFDEFHGNA YLENNYKVGE IKLPIPKLNQ	300
	DNQSTYIVEV PILEKENQTD KPSILPQFKR	350
	KVEKEKLSET GNSTSNSTLE EVPTVDPVQE	400
	M DGTIELYLPS GEVIKKNMAD FTGEAPQGNG	450
	F ENKPADSLPE APNEKPVKPE NSTDNGMLNP	500
	V DPVQEKLEKF TASYGLGLDS VIFNMDGTIE	550
LRLPSGEVIK KNLSDFIA		568
	FIGURE 29	
DLTEEQIKAA QKHLEEVKTS	HNGLDSLSSH EQDYPGNAKE MKDLDKKIEE	50
	C EKNAIIYPHG DHHHADPIDE HKPVGIGHSH	100
	/ YTGEELTNVV NLLKNSTFNN QNFTLANGQK	150 200
	/ KLITPDGKVL EKVSGKVFGE GVGNIANFEL	
DOPYLPGQTF KYTLASKDYI	EVSYDGTFTV PTSLAYKMAS QTIFYPFHAG	300
DIYLKVNPUF AVPKGTDALV	RVFDEFHGNA YLENNYKVGE IKLPIPKLNQ	329
GITRTAGNKI PVTFMANAYI	DNQSTYIVE (SEQ ID NO : 65) FIGURE 30	329
• • •	FIGURE 30	

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EVPILEKENQ TDKPSILPQF KRNKAQENSK LDEKVEEPKT SEKVEKEKLS ETGNSTSNST LEEVPTVDPV QEKVAKFAES YGMKLENVLF NMDGTIELYL PSGEVIKKNM ADFTGEAPQG NGENKPSENG KVSTGTVENQ PTENKPADSL PEAPNEKPVK PENSTDNGML NPEGNVGSDP MLDPALEEAP AVDPVQEKLE KFTASYGLGL DSVIFNMDGT IELRLPSGEV IKKNLSDFIA (SEQ ID NO : 66) FIGURE 31	50 100 150 200 240
DIDSLLKQLY KLPLSQRHVE SDGLIFDPAQ ITSRTARGVA VPHGNHYHFI PYEQMSELEK RIARIIPLRY RSNHWVPDSR NGVSRYIPAK NLSAETAAGI NGVSRYIPAK NLSAETAAGI SHKLGAKKTD LPSSDREFYN KAYDLLARIH QDLLDNKGRQ VDFEALDNLL ERLKDVSSDK VKLVDDILAF LAPIRHPERL GKPNAQITYT GDAYVTPHMT HSHWIKKDSL SEAERAAAQA YAKEKGLTPP STDHQDSGNT EAKGAEAIYN RVKAAKKVPL LATVKYYVEH PNERPHSDNG FGNASDHVQR NKNGQADTNQ TEKPSEEKPQ TEKPEEETPR EEKPQSEKPE SPKPTEEPEE ESPEESEEPQ VETEKVEEKL REAEDLLGKI QDPIIKSNAK ETLTGLKNNL LFGTQDNNTI MAEAEKLLAL LKESK (SEQ ID NO : 67)	50 100 150 200 250 300 350 400 450 500 550
DIDSLLKQLY KLPLSQRHVE SDGLIFDPAQ ITSRTARGVA VPHGNHYHFI PYEQMSELEK RIARIIPLRY RSNHWVPDSR PEEPSPQPTP EPSPSPQPAP NPQPAPSNPI DEKLVKEAVR KVGDGYVFEE NGVSRYIPAK NLSAETAAGI DSKLAKQESL SHKLGAKKTD LPSSDREFYN KAYDLLARIH QDLLDNKGRQ VDFEALDNLL ERLKDVSSDK VKLVDDILAF LAPIRHPERL GKPNAQITYT DDEIQVAKLA GKYTTEDGYI FDPRDITSDE GDAYVTPHMT HSHWIKKDSL SEAERAAAQA YAKEKGLTPP STDHQDSGNT EAKGAEAIYN RVKAAKKVPL DRMPYNLQYT VEVKNGSLII PHYDHYHNIK FEWFDEGLYE APKGYTLEDL LATVKYYVEH PNERPHSDNG FGNASDHV (SEQ ID NO : 68) FIGURE 33	50 100 150 200 250 300 350 400 428
GLYEAPKGYT LEDLLATVKY YVEHPNERPH SDNGFGNASD HVQRNKNGQA DTNQTEKPSE EKPQTEKPEE ETPREEKPQS EKPESPKPTE EPEEESPEES EEPQVETEKV EEKLREAEDL L (SEQ ID NO : 69) FIGURE 34	50
ASDHVQRNKN GQADTNQTEK PSEEKPQTEK PEEETPREEK PQSEKPESPK PTEEPEESP EESEEPQVET EKVEEKLREA EDLLGKIQDP IIKSNAKETL TGLKNNLLFG TQDNNTIMAE AEKLLALLKE SK (SEQ ID NO : 70) FIGURE 35	50 100 132

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000					
PYEQMSELEK NPQPAPSNPI DSKLAKQESL	RIARIIPLRY DEKLVKEAVR SHKLGAKKTD	RSNHWVPDSR KVGDGYVFEE	PEEPSPQPTP NGVSRYIPAK KAYDLLARIH		50 100 150 200 226
ITSDEGDAYV DSGNTEAKGA YHNIKFEWFD	TPHMTHSHWI EALYNRVKAA	KKDSLSEAER KKVPLDRMPY TLEDLLATVK	AAAQAYAKEK NLQYTVEVKN	•	50 100 150 200 203
IVIKITDQGY NEIKGGYVIK NAVAAARAQG ASELAAAEAY GENISSLLRE FIPYEQMSEL APNPQPAPSN GIDSKLAKQE RQVDFEVLDN YTDDEIQVAK	VTSHGDHYHY VDGKYYVYLK RYTTDDGYIF WNGKQGSRPS LYAKPLSERH EKRIARIIPL PIDEKLVKEA SLSHKLGAKK LLERLKDVSS LAGKYTTEDG	YNGKVPYDAI DAAHADNIRT NASDIIEDTG SSSSYNANPV	ISEELLMKDP KEEIKRQKQE DAYIVPHGDH QPRLSENHNL AQITSRTARG SRPEQPSPQS EENGVSRYIP YNKAYDLLAR AFLAPIRHPE DEGDAYVTPH	TVTPTYHQNQ VAVPHGNHYH TPEPSPSLQP AKDLSAETAA IHQDLLDNKG RLGKPNAQIT MTHSHWIKKD	50 100 150 200 250 300 350 400 450 500 550
PLDRMPYNLQ DLLATVKYYV SEPTHPESDE ENSVINAKIA	YTVEVKNGSL EHPNERPHSD KENHAGLNPS DAEALLEKVT KESQPAPIQ	IIPHYDHYHN NGFGNASDHV ADNLYKPSTD DPSIRQNAME (SEQ ID NO	IKFEWFDEGL RKNKADQDSK TEETEEEAED TLTGLKSSLL): 73) FIGURE 3	YEAPKGYSLE PDEDKEHDEV TTDEAEIPQV LGTKDNNTIS	650 700 750 800 819
IPYEQMSELE PNPQPAPSNP IDSKLAKQES QVDFEVLDNL TDDFIQVAKL LSEAERAAAQ LDRMPYNLQY	YAKPLSERHV KRIARIIPLR IDEKLVKEAV LSHKLGAKKT LERLKDVSSD AGKYTTEDGY AYAKEKGLTP TVEVKNGSLI	ESDGLIFDPA YRSNHWVPDS RKVGDGYVFE DLPSSDREFY KVKLVDDILA IFDPRDITSD	QITSRTARGV RPEQPSPQST ENGVSRYIPA NKAYDLLARI FLAPIRHPER EGDAYVTPHM TEAKGAEAIY KFEWFDEGLY	THSHWIKKDS NRVKAAKKVP EAPKGYSLED	50 100 150

LLATVKYYVE HPNERPHSDN GFGNASDHVR KNKADQDSKP DEDKEHDEVS

EPTHPESDEK ENHAGLNPSA DNLYKPSTDT EETEEEAEDT TDEAEIPQVE

NSVINAKIAD AEALLEKVTD PSIRQNAMET LTGLKSSLLL GTKDNNTISA

EVDSLLALLK ESQPAPIQ (SEQ ID NO : 74)

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FIGURE 39

450

500

550 568

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TOWNKADADE	KEDEDKEHDE	VSEPTHPESD	EKENHAGLNP	SADNLYKPST	50
AKKMANADODO	DTTDEXETED	VENSUTNAKT	ADAEALLEKV	TDPSIRQNAM	100
DIERIEFERE	DITUERETFO		TABEODYDIO	-	140
ETLTGLKSSL	LLGTKDNNTI	SAEVUSLLAL	PLESCENTIA		
/ARA ID NO	. 751				

GACTIGACAG AAGAGCAAAT TAAGACTAGT TAGAGCAGGT 50 ATACAGGTAA TOCCAAAGAA TAGAATCTTT TAGAATAGAAT 100 ATCCAGGTAA TOCCAAAGAA ATGAAAAATAGT 100 AAAATAGCT GCATTATGAA CAATAATGT TOCGAATAAA AACTGTTAA CACATAATTAA CCATAAAAAAA AACTGTTCTC 250 AGTAAAAATAGT AACTGTTAAA CACCAAAAAA TGGAATTATTAA CACCAAAAAAAATG CAAAAAAAATTAAAAAAAAAAAAAAAAAAAAAAAAAAA						
TARARCTAGT CATARTGGAT TAGATTCTTT TCGATCTCAT 150 ANACAGGTAA TGCAARGAA ATGAARAGAT TAGATAARAA AACCGGTAA 150 ARAATTGCTG GCATTATGAA ACAATTATGT 200 CGTGAATAAA GAATGATGAA CGATAAATTGT 200 AGTACACATC GAATGATGAA ACCCGAAGAA GGATTGATTGA AACTTTTAA ACCCGAAGAA GGATTGATTGA AAAAAAAATGGAC 350 GAATAAAGTT TATACTGGAB AAAAATTAAC GAATGATGAA TAGAGAAAAAT 400 AAAATTAATAA CACCAGATGG GAAGAAAAATT CACCAGATGG AAAATTAAAA 450 CGGTTAATTA ATTTACCAGG ACCAGATGGAA AAAAGTATTA CTCGAAAATTA CTCGAAATTA CTGCTAAATTA CTGCTAAAATTA CTGCTTAAAATTAC GAACAACTT AAGGAAAGTAT AAGGAAACTT AAGGAAACTT AAGGAAACTT AAGGAAACTT AAGGAAACTT AAGGAAACTAAAT CCAACCTCTT 700 AGAAAAGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	CACTTGACAG	AAGAGCAAAT	TAAGGCTGCG	CAAAAACATT	TAGAGGAAGT	50
ARACTECTA TECCAAAGAA ACAATATGGT GTCAAACGT AAAGATATGT 200 CGTGAATAAA GAAAAAAATG CGATTATTA TCCGCATGGA GATCACCATC 300 AGTAACTATG AACTGTTTAA ACCCGAACAA GGAATTGGT AAAAAAAAAA	TANANCTAGT	CATAATGGAT	TAGATTCTTT	GTCATCTCAT	GAACAGGATT	100
ARARTIGET GCATTATGAR ACASTATGGT GTCAAACGTG AAGTATUST CGTGAATAAA GAAAAAATG CGATTATTA TCCGCNIGGA GATCACCATC ATGCGGATCC GATTGATGAA CATAAACCGG TTGGAATTGG TGATCACTG AACTGTTTAA ACCCGAAGAA GGAGTTGCTA AAAAGAAGG GAATAAAGTT TATACTGGAG AAGAATTAC GAATTGTTA AATTGTTAA AAAATAAGTAC GTTTAATAAT CAAAACTTTA CTCTAGCCAA TGGTCAAAAA 450 CGCGTTTCTT TTAGTTTCC GCCCAGATGG GAATGATGT TAGGTAAAAA 450 CGCGTTTCTT TTAGTTACCAGG ACAAACATTA CTCTAGCCAA TGGTCAAAAA 450 CTGGTAAAGT ATTTGCGAGA GGAGTAGGGA AAAACATTA GAAAACTTA CTCGTTCAAAA AGGTTAAAAA TATTACCAGG ACAAACATT AAGTTGCAA CTTTGAATTA GAATTACCA AATGGCCAGT CAAACGATT TCTATCCTT CCATGCAGG GATCACCTT ATTACCAGG ACAAACATT TCTATCCTT CCATGCAGG GATACTTATT TAAGAGTGAA CCCTCAATTT CTCATCCTT CCATGCAGG GATACTTATT TAAGAGTGAA ACCAATTA TTACAGTT CAAACGATT TGCTTACAA AATGGCCAGT CAAACGATT TCTATCCTT CCATGCAGG GAACAACCA GAACGGCCG AAAACAATT TCTATCCTT CCATGCAGG GAACAACCA GAACGGCCG AAAACAATT TCTATCCTT CCATGCAGG GAACAACCA GAACGGCCG AAAAAAATTC CGATTCCGAA ATTAAACCAA GGAACACACA GAACGACGA ATCAAAATTC CGATTCCGAA ATTAAACCAA GGAACACACA GAACGACGA ATCAAAATTC CGATTCCGAA ATTAAACCAA AAAACTATA AGTTGGTGAA ATCAAATTAC CGATTCCGAA ATTAAAACCAA AAAACTATA AGTTGGTGAA AACCTTGTA AAAAACAAAAACT CAACCAACTA TACCACACAAC AACCAACTA TACCACACAAC AAAACTTGAT AAACCAACTAT TCTCACACA ATTAAAACCAA AAAACTATTA AACCAACTAA AAACTTGAT AAACCAATTA TCTCACCAC ATTTAAAACCAA AAAACTATAC AACGTTAGAA AAACTTGAT AAACCAATA AAACTTGAT AAACTTATA TTCCAACCA ATTAAAACCAA AAACTTACACAA AAACTTACACAA AAACTTACACAA AAACTTACACAAA AAACTTACACAAA AAACTTACACAAAAAATAAAC CAACTAACAATA AAAACTTACAAAAAATAAAC CAACTAACAATA AAACTTACAAAAAAATAAAC CAACTAACAATA AAAACTTACAAAAAATAAAC CAACTAACAATAAAC CAACTAACAATA AAAAATTACAAAAAAATAAAC CAACTAACAATA AAAAATTACAAAAAATAAAAC CAACTAACAATA AAAAATTACAAAAAAAA	ATCCAGGTAA	TGCCAAAGAA	ATGAAAGATT	TAGATAAAAA	AATCGAAGAA	150
CGTGAATAAA GAAAAAAATG CGATTGATTATTA TCCGCATGGA GATCACACTC 250 ATGCAGATCC GATTGATGAA CATAAACCGG TTGGATTGG 350 AGTAACTATG AACTGTTTAA ACCCGAAGAA GGAGTTGCTA AAAAAGAAGG 350 GAATAAAGTT TATACTGGAG AAGAATTAAC GAATTAATAA CACCGAAGAA GGATTGATAA 450 CGCGTTTCTT TATATCATAAC CACCAGATGG AGAAAAAATT AAGTAACTAA 500 GATCACACTT TATGCTAGAA AGACCAGATGG AAAAAATTAC GAGAAAAGTAT 550 CTGGTAAAGT ATTTGCAGAA ACCCAGATGG AAAAAGTATTG GAGAAAGTAT 560 CTGGTACACTT ATTACCAGG ACAAACATTT AAGTTACATA CCGTACATTT GAGACCCTT 700 AGATACATAA ATTACATTAA AGACGGCCGG AAATAAAATTA CCGTACATTT CCAACCCCTT 700 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	አአአአምፕርርማር	CCATTATGAA	ACAATATGGT	GTCAAACGTG	AAAGTATTGT	200
ATGCAGATCC GATTGATGAA CATAAACCGG TTGGAATTGG TCATTCTCAC AGTAACTGTTTAA ACCCGAAGAA GAGTTGCTA AAAAGAAGA AGAATAGTC GTTTAATAAT ACCCGAAGAA GAATTGTT AATTTGTTAA AAAATAGTAC GTTTAATAAT CAAAACTTTA CTCTAGCCAA TGGTCAAAAA ATGCTTT TTAGTTTTCC GCCTGAATTG GAGAAAAAAT TAGGTATCAA CGCGTTTCTT TTAGTTTTCC GCCTGAATTG GAGAAAAAAT TAGGTATCAA CGCGTTTCTT TTAGTTTTCC GCCTGAATTG GAGAAAAAAT TAGGTATCAA CGCGTTAAAGT AAATTAATAA CACCAGATGG AAAAGTATTG GAGAAAAATA CTTGGAAAGT ATTTACCAGG ACAAACATTT AGGTTAACCA GATTACCAGG ACAAACATTT AGGTTACCA AATGGCCAG CCAAACATTT AGGTTACCA GAATGAAGT ATTACCAGG ACAACATTT AGGTTACCA AATGGCCAG CAAACATTT AGGTTACCA GAGTAGAGT ACCCCCAGATGG ATTACCATT CCATCCAGA GATCACCAC AAGAACACATT AGGTTACAC AAGTGGAAA CCCCCCAATTG GCAGACCCCTT TAGGTTAGTC AGAGGTGTAG ATCAAATTAC CGATTCCTTT CCATCCAGGG GAACAACACATT AGAGGTACAA CCCCCCAATTG GCAGACCCCTCT TAGGTTAATAC AAGTGGAAA ACCAAAATAA CCCCTCAATTT GCAGTGCCTA AAGGAACTGA AAAAAGAAAAAAAAT CCACAACATT TGTGGAAATGA ATTAAACCAA GGAACACCA GACAGCACGG GAACACACTT TGTGGAAATTAC CCATCCTTTAGAACCA AAAAACAAAAAAAAT CCACAAATAAC CAGCATATATA TGTGGAAATGA CCTATCTTGG AAAAAGAAAAAAAAAAAT TGTGAAAAAAAT TGTGGAAAATAAAC CAGCATATATA TGTGGAAATGA AAGAAACAAAAAAAAAA	CCTCAATAAA	TRAGGGG	CGATTATTTA	TCCGCATGGA	GATCACCATC	250
AGTARATATE AACTGATTAA ACCCGARGAA GAGTTGCTA AAAAAAAAGG GAATAAAATT TATACTGAGA AAAAATTAAC GAATGTTGTT AAAATTAGTAA 450 AAAATAGTAC GTTTAATAAT CAAAAACTTTA CTCTAGCCAA TGGTCAAAAA 450 CGCGTTTCTT TTAGTTTCC GCCTGAATTG GAGAAAAAATT TAGGTATCAA 600 CTGGTAAAGT AATTGAGAA GGAGTAGGAA ATATTGCAAA CTTTGAAATTA 600 CTGGTAAAGT ATTGAGAGA GGAGTAGGAA ATATTGCAAA CTTTGAAATTA 600 GATCAACCTT ATTTACCAGG ACAACATTT AAGTATACTA 600 GATACTTACTA AATGGCAGT CAAACGATTT ATTTACCAGG ACAACGTTT TTAGTCATA 600 CGATACTTATT TAAGACTGAA ACCCCAAATTT TAGGTACACA 600 CGATACTTATT TAAGACTGAA ACCCCAAATTT TAGGAAAGGTTA TAGAGTGAAAAAATTAC CCATCCTTT TAGGTAAAA 600 CGATACTTATT TAAGACTGAA ATCAAATTCA TGGAAATGCT TATTACACGA 800 CGATACTTATT TAAGACTGAA ATCAAAATTAC TGGAAATGCT TATTACACGA 800 CGATACTTATT GAACGGCCGG AAAACAATTC TGGAAATGCT TATTACACAA 900 CGACAACCA GAACGGCCGG AAAACAATTAC TGGAAATGCT TATTACACAA 900 CGACAACCA GAACGGCCGG AAAACAATTAC TGGAAATGCT TATTACACAA 900 CGACAACCA GAACACAAT CGACTTATT TGTGAAATGC TATTAAACCAA 900 CGACAACCA GAACACAAT CGACTTATAT TGTGAAAGT CCTATCTTGG AAAAAAAAACAAAAACAAAAACAAAAACAAAAACAAAAAA	ATCCACATCC	CATTGATGAA	CATAAACCGG	TTGGAATTGG	TCATTCTCAC	300
GARTARAGTT TATACTGGAG AAGRATTAC GARTATTGTT AATTITITAA ARAATAGTAC GTTTAATAAT CALAACTTTA CICTAGCCAA TGGTCAARAA CGCGTTTCTT TTAGTTTTCC GCCTGAATTG GAGAAAAAT TAGGTATCAA CACCAGATGG AAAAATTATCAA CACCAGATGG GAAGAAAAAT TAGGTATCAA CGGGTTCAACT AATTAGCAGGA CACACAGATG AAAAATTATCCA GAATTATCCA GAAGTAAGTT ATGATGGACAA AATTACCAAA CGGATTACCAC GAAGTAGTT ATGATGCAAA CGGATTACCAC GAAGTAGTT ATGATGCACA CACACACTT TAGAGTGAAA CACACAGTT CCTATCCTTT CCATCCAGG CGATCACACA CACACACTT AAGAGTGAAA AATTACCACA CACACACAC CGAACACCAC CAACACACAC CACACACA	AIGCAGAICC	AACTGTTTAA	ACCCGAAGAA	GGAGTTGCTA	AAAAAGAAGG	350 ·
ARARTAGTAC GTTTAATAAT CARAACTITA CTCTAGCCAA TGGTCAAAAAA 500 CGCGTTTCTT TTAGTTTTCC GCCTGAATTG GAGAAAAAAT TAGGTAAAAA 550 CTGGTAAGA AAATTAATAA CACCAGATGG AAAACTATT GAGTATACCAG AAAACATTT ATGTTACCAGG ACAAACATTT TAGGTATACCA GAGAAACATTT TAGGTATACCAG AAACGATTT TAGGTATACCA GAGAAACATTT TAGGTATACCA GAGAAACATTT TAGGTATACCA GAGAACAACATT TAGGTATACCA GAGAAACATTT TAGGTACACA AATGACCAGATG AAACACATTT CCCAACCTCTT 700 CAGACACACATT TAGAGTACAA AAGTAACTA CCCAACCTCTT 700 CAGACACACA AATGACTACAA AAGTAACTA CCCAACCTCTT 700 CAGACACACA AATGACTACAA AAGTACCAA AAGTACCAA AAGTACCAA TAGACACACA CACCACATT TAGAGTGAA CCCCCAATTT GCCATGCCAGG 750 CAAACGAATTA TAGAGTGAAA AAGAACACAA TAGACCAACAC GACCACCACA AATAAAAATT CCGAATCCAA TAGACCAACA GACCACACA CGACTACTTATAT TAGGAAACACAA AAACCCAACA AAACCAACACA AAACCCAACA AACCCAACAA	AGIAACIAIG	TATACTCCAC	AAGAATTAAC	GAATGTTGTT	AATTTGTTAA	400
GGGTTTCTT TIAGTTTCC GCCTGAATTG GAGAAAAAT TAGGTATCA TATGTAATA AAATTAATAA CACCAGATGG AAAGTATTG GAGAAAGTAT GGATAACCTT ATTTGCAGA GAGATAGGGA ATATTGCAAA CTTTGAATTA GAATTACCA GAAGTAGGTA ACAAACATTT AGGTTACAA ATGGCCAGT CAAACGATTT TCGCTTCAAA GATTATCCA GAAGTAGGTA CCCTCAATTT CCAACCCTCTT TAGCTTACAA AATGGCCAGT CAAACGATTT TCTATCCTTT CCAACCAGGG GATACTTATT TAAGAGTGAA CCCTCAATTT GCAGTGCAGG GGATACTTATT TAAGAGTGAA CCCTCAATTT GCAGTGCAGG GGACACACCA GAGCGCCGG AAATTACC CGATCCCAA ATTAACCAA AGTTGGTGAAA AGTGGTGAAA TCAAATTCA TGGAAAATTCC TGCTTTAGAAA GGAACAACCA GACGGCCGG AAAATTAC CGATCCGAA ATTAACCAA GGACACACCA GACGGCCGG AAATAAAATT GGACATATTATA AGAGTGAA CCCTCAATTT TGGAAATGCT TCATGGCAAA AGAAAACACTA TAAAACTGAA TAAAACTTAAT TGGAAAATAC CCTGTAACCT TCATGGCAAA AAAACCAAGTA TCAAACTGAT AAAACTTGAT TGGGAAGGTA CCTGTAACT TCATGGCAAA AATAAAACCAA AAAACTTGAT TATGGAAAAACT TCTGGAAAACT TCTGAAACACAA ATTTAAAAGG AAAACTTGAT TCTGCACAA ATTTAAAAGG 1050 CTAGTAATTG GACGATCAAT AAAACTTAATA TATGACACAA ATTTAAAAGG AAAACTTGAA AAAACTTAATA TTCTGCACAA ATTTAAAAGG 1050 CTAGTAATATG GACGAACAAT TTTACAGAGA AATTTACCACAA ATTTAACAGAA AATTTACCAAA AAACTTAATA TTTACCACACA ATTAAAAGG AAAAACTTA TTTACCACACA ATTAAAAGG AAAACCAAAAACT TTTACCACACA ATAAACCAAAA AACTTAAAGA AACTTAAGAGAA AACTCAACAA AACTCAACAA AACCAACAA TTTACACGAAA AACCAACAA TTTACACGAAA AACCAACAACA TTTACACGAAA AACCAACAA TTTACACGAAA AACCAACAA TTTACACACAA AACCAACAA AACCCACAA AACCCACAA AACCCACAA AACCCACAA AACCCACAA AACCAACAA	GAATAAAGII	CTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	CADAACTTTA	CTCTAGCCAA	TGGTCAAAAA	450
TATGCTAGTA AAATTAATAA CACCAGATGG AAAAGTATTG GAGAAAGTATT CTGGTAAAGT ATTTGGAGAA GGAGTAGGGA ATATTGCAAA CTTTGAATTA 600 GATCAACCTT ATTTACCAGG ACAAACATT AAGTATACTA TCGCTTCAAA AGGATTATCCA GAAGTAGTT TAGGATTACCA GAAGTAGTT TAGGATTACTA AATGGCCAGT GATACTTATT TAAGAGTGAA CCCCTCAATTT CTATCCTTT CCATGCAGGG GATCACTATAT AAGTGGTAAA TGCTTAGTT TAAGAGTGTAA ATGAACGATTT TCTATCCTTT CCATGCAGGG GATAACTATAA AGTTGGTGAA ATGAACTATT GCGATCACTA AAGGAACTGA 800 GGAACAACCA GAACGGCCCG AAAATAAAATT CGGAAATGCT TATTTAGAAA 950 GGAACAACCA GAACGGCCCG AAAATAAAATT CGGAATCATT GAAAACTAAT TGGGAAAACT TCATGCACA ATTAAAACCAA 950 GGACCAACCA GAACGACCA CAACCAATT TTCTACCACA ATTAAAACCAA 950 GACCAACTATTA AAAACTAACT AAAACTTGAT GAAAACTATC CCTGTTAGCCT CCATCTTGG 1000 GACTAGTGGG AAGGAACACC CAACTATATA TTCTACCACCA ATTAAAACGA 950 GACCAACGA AAACTGAAT AAAACTTGAT GAAAACTTGAT CAAACCTACA AAACTTGAT TTCTACCACA ATTAAAACGA 1100 GACTAGTGAG AAGGTAGAAA AACTAACCT TCTACACACA AATTAAAAGG 1050 GACTAGTGAG AAGTTAGAAA AACTAACGA AATTTACAGGAG AAGTAACTA TCTGAAACT GGGAATAGTA 1150 GTTTAATATG GACGAACAA TTGAATTATA TTTACCATCA GAGAAACCTA 1250 GTTTAAAAAGAA AATTTGCTGA AAGTTATATA TTTACCATCA GAGAAACTCA 1250 GTTTAAAAAGAA AATTTGCTGA AACTTAACGG AAAACCAGA AACTCAACGG ATTAACCACA CAGCAGATC TTTACCACAA AACCCACAC AAAACCAGA AACTCAACGG ATAATGGAAA CAGCACACAC 1350 GAAAAACCTGT AAAACCAGAA AACTCAACGG ATAATGGAAA TTTACCACACA CAGGTAGAAC 1450 CAAACACAGA AACCCAGAA AACTCAACGG ATAATGGAAA TTACCACAGA CAGGAAAAATTA CAAACCAGAA AACTCAACGG ATAATGGAAA TTACCACAGA CAGTTGAAACCA AACCCAGAA AACCCACACA AACCCACACA CAGCAGAATT TATACCACAG ATAATGGAAA TTACCACAGA AACCCAGAA AACCCACACA CAGCAGAAAATTA AACAACTTAT AACACATCA GAAAAAAATTA AACAACTTAT AACACCAGA AACCCACAC CAGCAGAATT AACACATCA GAAAAAAATTA AACAACTTAT AACACATGA CAGCTAGATT AACACATCA GAACAAAAATTA AACAACTTAT AACACATCA CAGCAGAAAATTA AACACATTA AACACATCA CAGCAGAAAAATTA AACACATTA AACACATCA CAGCAGAAATTA CAAACCACAG AACCAACAC TAAACCACATC CAAACCACAC CAAACCACAC CAAACCACAC CAAACCACAAC CAAACCACAAC CAAACCACAAC TAAACCACAAC TAAACCACAAC AACCAACAC TAAACCACAAC AACCAACAC CAAACCACAAC TAAACCACAC AACCAACAC TAAACCACAC AACCAACAC	AAAATAGTAC	GIIIMMINTO	CCCTGAATTG	GAGAAAAAT	TAGGTATCAA	500
CTGGTAAAGT ATTTACCAGG ACAAACATTT AAGTATACTAA CTTGAATTA GATCAACCTT ATTTACCAGG ACAAACATTT AAGTATACTA TCGCTTCAAA GATTATTACCA GAATAAGTT ATTTACCAGG ACAAACATTT AAGTATACTA TCGCTTCAAA GATTATTACCA GAATAAGTT ATTTACCAGGT CAAACGATT TAGCTTACAA AATGGCCAGT CAAACGATT TAGCTTACAA GATGGCAGT GATACTTATT TAAGAGTGAA CCCTCAATTT GCAGTCCAGG GATACTATAT GAGTGGTATA AGGTGGTATA AGGTGGTATA AGGTGGTATA AGGTGGTATA AGGTGGTAA ATGAATTAC GAAACACAA GAACACAA GAACACCA GAACGACCA GAACGACCA GAACGACCA GAACGACCA GAACGACCA GAACGACCA GAACACAAT CCGACTTATTC GACAACCAAC GAACACACA GAACACACAC	CGCGTTTCTT	AAATTAATAA	CACCAGATGG	AAAAGTATTG	GAGAAAGTAT	550
GATCAACCTT ATTACCAGG ACAACATTT ATGATACTA TAGATTACTA TAGATTACTACA ATGATTACCA GAAGTAGGT ATGATTACAGTT TCATCCTTT CCAACCTGTT TAGATCTATT TAAGACTGAA CCCTCAATTT TCATCCTTT CCATCCTGT AGGAACACCA AGGACACCA AACACATTT TCTATCCTTT CCATCCTGAGG 750 AGGACACACCA AGGACTGAA ACCAACATTA TAGACCAAA AGGACCACA AGGACACCA AACACACACA ACCACACACA	TATGCIAGIA	AMMITAMIA	GGAGTAGGGA	ATATTGCAAA	CTTTGAATTA	600
AGATTATCCA GAAGTAAGTT TAGATGGTAC ATTTACAGTT CCAACCAGGG 750 GATACTTATT TAAGAGTGAA CCCTCAATTT GCATGCAGGG 750 GATACTTATT TAAGAGTGAA CCCTCAATTT GCATGCAGGG 750 ATAACTATAA AGTTGGTGAA ATCAAATTAC GCAGTGCCTA AAGGAACCAA 900 GGAACAACCA GAACGCCG AAATAAAATT CGACTTATTTT GAAACCAA 900 GGAACAACCA GAACGCCG AAATAAAATT CGACTTATTTT GAAACCAA 950 GGACAACAAC GAACGACTA TAGAACTTAT TGTGGAAACT TCAAGCACA 950 AATAAACTATA AAACCAAAT AAACCAACTA TTCTACCACA ATTTAAACCAA 950 AATAAAACACAA AAACCAACTA TTCTACCACA ATTTAAAACCAA 950 AATAAAACCACAA AAACCTGAT TTCTACCACA ATTTAAAACCAA 950 AATAAAACCACA AAGAAAAACT CAAACTACT TTCTACCACA ATTTAAAACCAA 100 GACTAGTGAG AAGGTAGAA AAACCTCCTA AAAACCAACA AAAACCTGA AAAACCTGAA AAGTTACTCA AAGTTACACA AAATTACCAA AAATTACCAA AAATTACCAACAA AAATTACCAACAA AAACCAACAA AATTTGCTGA AAGTTATACA TTTAACACAGA AAAACCAACAA AAAACCAACAA AAAAACCAACA AAAAACCAACAA	CIGGIAAAGI	ATTIGGAGAA	ACAAACATTT	AAGTATACTA	TCGCTTCAAA	650
TAGCTTACAA AATGGCCAGT CAAACGATT TCTATCCTTT CCATGCAGG 750 GATACTTATT TAAGACTGAA CCCTCAATTT TGGAAACGAT AAGGAACTGA 800 TGCTTTAGTC AGAGTGTTG ATGAATTTC TGGAAACGAT TATTTAGAAA 850 TGCTTATATA AGTTGGTGAA ATCAAATTAC CGATTCCGAA ATTAAACCAA 900 GGAACAACCA GAACGCCGG AAATAAAATT CGAACTACAT TGGAAAACCTA TCATGGCAAA 950 TGCTTATTG GACAACCAGT AAAACCAAGT TCTGGAACCA ATTAAAAGG 1050 AAAAAAAAAACTGAA AAACCAAGT AAAACCAAGT TCTGGAAACCAA AAGAACAAGT AAAACCAAGT AAAACCAAGA AATTAAAACCAA AATTAAAAGAA AATTTGCTGA AAAGTTACTG GAAGTTACT GAAGTAAAAC CAACTGAAA AATTTGCTGA AAGTTACTG GAAGTTACT GAAGTTACT GAAACCAAGA TCTAACAGG AAAAACCTGA CAACCAACA AAAACCTGA TCTACACGA AAAACCTCA AAAAACCTGA CAACCAACA AAAACCAAGA AACCAAGAA AACCAAGAAAAAAAA	BATCAMCCII	CANCTABGTT	ATGATGGTAC	ATTTACAGTT	CCAACCTCTT	700
GATACTTATT TAAGAGTGAA CCCTCAATTT GCTTTAGTC AGAGTGTTGA AGATGTTCA AGATGTTGA ATCAAATTAC AGATGCTTAA AGTTGGTGAA ATCAAATTAC CGACTCACAC GGACAACCCA GAACGGCCGG AAATAAAAAT CCAACTATTG GACAACCAC AAACACAACT AAAACACACA AAACACACAC	AGATTATCCA	NATOCICACT	CAAACGATTT	TCTATCCTTT	CCATGCAGGG	750
TGCTTTAGTC AGAGTGTTTG ATGAATTTCA TGGAAATGCT TATTTAGAAAA 900 GGAACAACCA GAACGGCCGG AAATAAAATTAC CGATTCCGAA ATTAAAACCAA 950 GGAACAACCA GAACGGCCGG AAATAAAATTAC CGATTCCGAA ATTAAAACCAA 950 AAAAAGAAAA TCAAACTGAT CGACTTATAT TGTGGAAGTA CCTGTATCTTGG 1000 AAAAAGAAAA TCAAACTGAT AAACCAAGTA ATTAAAAGG 1050 AAAAAGAAAAAATT CAAACTGAT AAACCAAGAA AAGAAAAACTT TGTGGAAACT GGAAATAGTA 1100 AACTAGTAGGA AATTTGCTGA AAGACAACCAAA AAGAAAAACT TTCTGAAACT GGGAATAGTA 1200 AAAAATAAAC AAGAAAAACT CAAGAAGAAC TTCTGAAACT GGGAATAGTA 1250 AAGAATAAAC CACTGAAAA TTGGAAAAACT TTTACCATCA GGAAAATGGT 1350 AAAAACCAACA ATTTACCAGAA AAGAAAAACT TTTACCATCA GGAAATAGT 1350 AAAAACCAACA AAAAACCAAGAA TTTACCAGAA AAGAACAATAC CAGCAAGAAC TTTACCAGAA AAGAACAACCAAAA 1400 CCAACCAACA GAAAAAAAAC CAGCAAGAAC CAGCAAGAAC CAGCAAGAAC TTTACCAGAA AACCAAACA AACCAACAAC AACCAACAA AACCAACAA	TAGCTTACAA	TARGCCAGI	CCCTCAATTT	GCAGTGCCTA	AAGGAACTGA	800
ATAACTATAA AGTTGGTGAA ATCAAATTAC CGATTCCGAA ATTAAACCAA GAACGCCGG AAATAAAATT TCATGGCAAA 950 GGAACAACCA GAACGGCCG AAATAAAATT TCATGGCAAA 950 TGCTTATTTG GACAATCAAT CGACTTATAT TGTGGAAGTA CCTATCTTGG 1000 AAAAAGAAAA TCAAACTGAT AAACCAAGTA TTCTACCACA ATTTAAAAGG 1050 AATAAAAGCAAA AAACTTGAT AAACCAAGTA TTCTACCACA ATTTAAAAGG 1100 GACTAGTGAG AAGGTAGAAA AAACTTGAT TGTGGAAGTA AAGAACAAAA 1100 GACTAGTGAG AAGGTAGAAA AAACTTGAT AAACTTGAT AAAGTTAGTA AAGGTACAAA ATTTAAAAGG 1100 GACTAGTGAG AAGGTAGAAA AAGAAAAACT AAGGTACCAAA AAAACTGAT TTTACCAGCA AAAAATTAAC CAGTGGAACAA TTTAAAACGAA AAATTTACAAGAA AAAAACTAAA TGGAAAAGTA TTTACCAGCA GAAAATGAAC CAGCAGAATC TTTACCAGCAG AAAAACCTGA AAAACCAGAA AACTCAACGG AAAAACCAGAA AACTCAACGG AACCAACAG GAAAAAAACT AAGAAAAAATT AGGAAAAAATT AGGAAAAAATT AGGAAAAAATT AGAACAAAG 1450 GAAAGGGAATG TGGGGAGTG CCCTATGTTA AAGAAAAAATT AGAACAAGG CTTAGAATAG CTTAGATGAT TAGAGGAAAAATT AGAAAAAAATT ACAGCTAGTT AAAACCAGAA AACTCAACGG AATAATGGAAG CTTAGAACGG AACCGAACAG ATTACGTT CAAACCAGA AACCAACAG ACCAACAG ACCAACAGA AACCAACAG ACCAACAGA AACCAACAG ACCAACAGA AACCAACAG ACCAACAGA ACCAACAGA ACCAACAGA AACCAACAG ACCAACAGA ACCAACAA	GATACTIATI	LANGAGIOAA	ATGAATTTCA	TGGAAATGCT	TATTTAGAAA	850
GGAACAACCA GAACGGCCGG AAATAAAATT CCTGTTAACCT TCAIGGARAA TGCTTATTTG GACAATCAAT CGACTTATATAT TGTGGAAGTA CCTATCTTGG 1050 AAAAAAGRAAA TCAAACTGAT AAACCAAGTA TTCTACCACA ATTTAAAAGG 1050 AATAAAAGCAA AAGAAAACTC AAAACTTGAT GAAAAGGTAG AAGAACCAAA 1100 GACTAGTGAG AAGGTAGAAA AAGAAAAACT AAGAAAAACT AAGAAAAACT AAGAAAAACT AAGAAAAACT AAGATTACCACA AATTTACAACA AAGAAAAACT AAGAAAAAACT AAGAAAAAACT AAGAAAAAGTA AAGAAAAAACT ATGAAACACAA AACTTAGAGAA AACTAAAGAA AACTAAACAGAA TTTAACAATCA GAGAAAAGTA TTTAACAATCA GAGAAAATAAC CAACCAACA GAAAAAACACAGA AACTCAAACG GAAAATAAAC CAACCAGAA AACTCAAACG AAAAACCAGAA AACTCAAACG AAAAAACCTGT AAAACCAGAA AACTCAAACG AAAAAACCTGT AAAACCAGAA AACTCAAACG GAAAAAAAAT AGGAAAAAATT AAGAGAAAAATT AAGAAAAAATT AAGAGAAAAATT AAGAGAAAAATT AAGAGAAAAATT AAGAAAAAATT AAGAGAAAAATT AAGAAAAAATT AAGAAAAAATT AAGAAAAAATT AAGAAAAAATT AAGAAAAAATT AAGAGAAAAATT AAGAAAAAATT AAGAAAAAAATT AAGAAAAAAAA	TGCTTTAGIC	AGAGIGITIG	ATCAGATTAC	CGATTCCGAA	ATTAAACCAA	900
TGCTTATTTG GACAATCAAT CGACTTATAT TGTGGAAGTA CCTATCTTGA AAAAAGAAAA TCAAACTGAT AAAACTAGAT ATTCACCACA ATTTAAAAAGG AATAAAGCAC AAGAAAACTC AAAACTTGAT GAAAAGGTAGA AAGACCAAAA 1100 GACTAGTGAG AAGGTAGAAA AAAACTTGAT GAAAAGGTAGA AAGACCAAAA 1150 CTAGTAATTC AACGTTAGAA GAAGTTCCTA CAGTGGATCC TGTACAAGAA 1200 GTTTAATATG GACGGAACAA TTGAATTATA TTTACCATCA GAGAAATGTT 1250 GTTTAATATG GACGGAACAA TTGAATTATA TTTACCATCA GGAAAATGTCT 1300 GTAGAAAAAAACCAACA CATCTGAAAA TGGAAAAATAAAC CATCTGAAAA CAGCAAGATC AAAAACCTGT AAAAACCAGAA AACTCAACGG AAAAACCTGT AAAAACCAGAA AACTCAACGG ATTACCAGGA GCACCAAAACG 1450 CCAACCAACA GAAAATAAAC CACCAGAA AACTCAACGG ATAATGGAAT GTTGAATCA AACTCAACGG ATAATGGAAT GAACCAGAA AACTCAACGG ATAATGGAAT GAACCAGAA AACTCAACGG ATAATGGAAT TAGAGGAACCA TAGAGGAACC 1550 TCCAGCAGTA GATCCTGTAC AAGAAAAAATT AGAAAAAATT AATAGGATGA ACCGATAGTT 1600 ACGGATTGGC CAAGCAGA CCTTAGAAAA AGCAAAAATT AATAGGATGA AACGATTGAA AGCAACAATC CGTTATCGTT CAAACCATTG GGTACCAGAT TCAAGACCAG 1750 AGGAAACCAAG TCCACAACCG CCAAACCATTG GGTACCAGAT TCAAGACCAG 1750 AGGACAAGT CTCACACAG TCCAAACCATTG GGTACCAGAT TCAAGACCAG 1750 AGGACAAGT GCCACAACC TCCAAACCATTG GGTACCAGAT TCAAGACCAG 1750 AGGACAAGT GCCACAACC TCCAAACCATTG GCAACCATTG TTATGTCTT GAGGAAACT TTCAGCAAGA TCCCACAACCG CCAAGCAACC TCCAAACCAT TCCAAGAACC 1950 AGCACAAGTTG ACTGACAGA ACTCCAGAAC TTTCAGCAGA ACCGAACCT 1800 ACCCACAAGTTG ACTGACAGA ACTCCAGAAC TTTCAGCCAGA TTTCAGCCAG ACCTCAAGGA ACTCCAAGAAC TTTCAGCCAG ACTCAAGGA ACTCCAAGAAC TTTCAGCAAG ACCGAACCT TAGAGCAACC TCCACAAGAAC TTTCAGCAAG ACCGAACCT TAGAGCAACC TCCACAAGAAC TTTCAGCAAG ACCGAACCT ACTGAGAAC ACTCCAAGAAC TTTCAGCCAAG ACCGAACCT TAGAGCAACC TCCACAAGAAC TTTCAGCAAG ACCGAACC TCCACAAGAAC TTTCAGCAAG ACCGAACCT TAGAGCAACC TCCACAAGAAC ACCAATC TCCACAAGAAC ACTCCAAGAAC ACTCCACAG ACCAACCATC ACTCAGAAC ACTCACAGA ACCAAATC CCACAAGAAC ACCAAATC CAACCAATC ACTGACAAC ACTCAAGAA ACCAAATC CAACCAATC ACTGACAAC ACTCAAGAA ACCAAATC CAACCAATC ACTGACAAC ACTCAAGAA ACCAAATC CAACCAATC ACTAGAAAAACCAAC ACCAATTC CAACCAACCATC ACTAGAACAAC ACCAATTC CAACCAACCATC ACTAGAACAAC ACCAAATC CAACCAATC ACTAGAACAAC ACCAAATC CAACCAATC ACTA	ATAACTATAA	AGIIGGIGAA	TTAAAATT	CCTGTAACCT	TCATGGCAAA	950
AAAAAGAAAA TCAAACTGAT AAACCTAGAT ATCTACCACA ATTTAAAAGGA 1100 RATAAAGCAC AAGAAAACTC AAAACTTGAT GAAAAGGTAG AAAACTTGAT AAAACTTGAT TTCTGAAACT GGGAATAGTA 1150 CTAGTAATTC AACGTTAGAA AAGATTATGAT ACGGTAGATC TGTACAAGAA 1200 AAAGTAGCAA AATTTGCTGA AAGTTATGAG AAGTTATGAG AAATTTAATATG GACGGAACAA TTGAATTATA TTTACCATCA GGGAATAGTA 1250 TTAAAAAGAA TATGGCAGAT TTTACAGGAG AAGCACCTCA AGGAAATGGT 1300 CTAACCAACA GAAAATAAAC CATCTGAAAA TGGAAAAGTA TCTACCAGAA CAGTTGAGAA 1400 CCAACCAACA GAAAATAAAC CAGCAGATTC TTTACCAGGA CAGTTGAGAA 1400 CCAACCAACA GAAAATAAAC CAGCAGATTC TTTACCAGGA CAGTTGAGAA 1400 CCAACCAACA GAAAATAAAC CAGCAGATTC TTTACCAGGA CAGTTGAGAA 1400 CCAACCAACA GAAAAAAAATT AACACCAGAA AACTCAACGG GAACCAACG 1450 CCAACCAGAG TGGGGAATAGT CACTCAGAA AACTCAACGG GATCCAGAAC 1550 TCCAGCAGTA GATCCTGTAC AAGAAAAAATT ACAGCTAGTT 1600 ACGGAACCTT CACACACGA ACTCAACGA AACACAATTC CAGACCAGA 1550 ACGGAACCTT CACACACGA ACTCAACAGA AACTCAACGA TCCACAACCAG 1750 AGGAAACAACT CCCACAACCAG ACTCCAGACCT TCCAAGAACACT TCCACAACCAG TCCAAACCAGT TCCACAACCAG ACTCAAGAACATT TCCACAAGAA ACTTACCCAAGAACT TTTCAGCAGA AACACCAACCT TCCAAACCAG TTTCAAGACCAG TCCAAACCAG ACTCAAGAAC TTTCAAGAAAATT TCCACAAGAA ACTGACCAGA ACTCAAGAA ACTCAACGAACT TCCACAAGAA ACTCAACCAG ACTCAAGAACT TTTCAGCAGA AACAGCAGCA 1950 GGCATTGATA ACTGACACAG ATTCACCAAG ATTTACTTC ATAAAAGTA ACTGACCAGA ACTCAAGAA ACTTACCTAGA ACTCAAGAACTT TACAAAAGGT ATTCACCAAG ATTTACTTTA TATAAAAGC CCTTCTAGAAAAGTC ATTTGAGAAAAGTC ATTTGAGAAAATTA CCTGATTACC AACAAATTC CCAAACTACC CAAACTACC CCAAACTACC CCAAAC	GGAACAACCA	CAACOGCCGG	CGACTTATAT	TGTGGAAGTA	CCTATCTTGG	1000
ARTARAGCAC GACTAGTGAG GACTAGTGAG GACGAGACA AAGGAAAACT CAAGTAGAAA AAGGAAAACT CAAGTAGAAA AAGGAAAACT CAAGTAGAAA AAGGAAAACT CAAGTAGAAA AAGTAGCAA AATTTGCTGA AAGTTAGAA GAAGTTCTA AAGTTAGAA GAAGTTCTCA AAGTTAGCAA AATTTGCTGA AAGTTATATA TTTACCATCA GGAAAATCAAA CATCTGAAAA TATGGCAGAT TTTACAGGAG GAAAATAAAC CATCTGAAAA CACCAACA AAAACCAGT GAAAACCAGAA AACCCAACA AAAACCAGT GAAAACCAGAA ACCCAACA AAAACCAGT GAAGGGAAAT CCACCAACA AAAACCAGAA ACCCAACA AACCCAGCA CACCAACA CACCAACA CACCAACA AACCCAGCA CACCAACA CACCAACAC CACCAC	TGCTTATTTG	GACAAICAAI	DDDCCDAGTA	TTCTACCACA	ATTTAAAAGG	1050
GACTAGTGAG CTAGTAATTC AACGTTAGAA GAAGTTCCTA CAGTGGATCC TGTACAAGAA AATTTGCTGA AAGTTATATG GACGGAACAA TTGAAATATA TTTACCATCA GGGAAAGTTCA TTAAAAAGAA TATGGCAGAT TTTACAGGAG GAAAATAAAC CAACCAACA GAAAAACCTGT AAAACCAGAA AACCAGAA AACCAGAAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAA AACCAGAAAAAC CAAACCAGAA AACCAGAAAAAAC CAAACCAGAA AACACATTA AAGAAAAATT AGAAAAATT AAGAAAAATT AAGAACAAG CAGTGGAGA AACACATTG AAGAACAAC CAGTGGAGA AACACATTG AAGAACAAC CAGTAGAAA AACCATTA AAGAACAAC CAGAACAAC CAGTAGAAA AACCATTAAAA AAGAAAAATT AAGAAAAATT AAGAAAAATT AAGAACAAG CAGAACAACAT CAAACCAATG GACAAACCATG GACAAACCATG CAAACCAACC CAACCAACC CACCAACCAC CACCAACCAC CACCAACCAC CACCAACCAC CACCAC	AAAAAGAAAA	DACABACIGAI	ADACTTGAT	GAAAAGGTAG	AAGAACCAAA	1100
CTAGTAATTC AACGTTAGAA AATTTGCTGA AAGTTATGG GTTTAATATG GACGGAACAA TTGAAATATAA TTTACCATCA GGAGAAGTCA TATAGCAGAA TATGCAGAA TTGAAAAGTA TATGCAGAA CAACCACCA GAAAATAAAC CAACCACAC AAAACCTGT AAAACCAGAA AACTCAACGG GAAGGAATT TATGCAGAG TAGGGGAGTGA CCCTATGTTA ACGCAGAT TAGGCAGAT TAGGAAAATT TAGAACAGAA ACTCAACGG ATAATGGAAT TAGAGACAGA ACTCAACGG TAGGGAATG TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAATT ACAGCTAGTT ACAGCAGAT CAAGTGGAGA TAGACCAGA TAGACCAGA TAGACCAGA TAGACCAGA TAGACCAGA TAGACCAGC TAGACCAGC TAGACCAGC TCCAACCAG GCACCAAACC TCCAACCAG TCCAACCAGC TCCAACCAG TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TCCAACCAGC TTATTCTT GAGGAAATT TTTCACCAGA ACTGACCAGC TTATTCTT TTTCACCAGA ACGACCAGC TTCCAACCAGC TTCCACACCAGC TTCCACACCAGC TTCCACACCAGC TTCTCTCAACCAGC TTCCACACCAGC TTCCACACCAC TTCCACACCAGC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACCACCAC TTCCACCACCAC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACACCAC TTCCACCACCAC TTCCACCACCAC TTCCACCACCAC TTCCACACCAC TTCCACACCAC TTCCACCACCAC TTCCACCACCAC TTCCACC	AATAAAGCAC	ANGRARACIC	AAGAAAACT	TTCTGAAACT	GGGAATAGTA	1150
AAAGTAGCAA AATTTGCTGA AAGTTATGGG ATGAAGCTAG AAAATGTCTT GTTTAATATG GACGGAACAA TTGAATTATA TTTACCATCA GGAGAAATGA TTAAAAAGAA TATGGCAGAT TTTACAGGAG AAGCACCTCA AGGAAATGGT GAAAATAAAC CATCTGAAAA TGGAAAAGTA TCTACTGGAA CAGTTGAGAA AAAACCAGCA AAAACCAGAA AACTCAACCG ATAATGGAAT GTTGAATCCA 1500 TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAACAAATT AGACCAGCA TTGAATCCA 1500 TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAACAAATT ACAGCTAGTT 1600 ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA ACGGATTGAA AGTTATTCA ATATGGATGG AACGATTGAA TCCACAACCG CCTATGTTA AGAACAATT CTGATTCAT 1700 ACGGAAGCTAG CCTTACGTT CAAACCATT GGTACCAGCA TCCACAACCG TCCAAACCAT TCCACAACCG CTCAACCAGC CCTAGTTA GAACACATT GGTACCAGCA TCCACAACCG TCCAAACCAT TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCG TCCAAACCAT TCCACAACCG TCCAAACCAAT TCCACAACCG TCCAAACCAAT CCAATTGAT TCCACAACCG TCCAAACCAAT TCCACAACCG TCCAAACCAAT TCCACAACCT TAGAGCACCA TCCAAACCAT TCCACAACCG TCCAAACCAAT TCCACAACCT TCCACAACCA TCCACAACCA TCCACAACCA TCCACAACCA TCCAAACCATT GAGAACATTGT TCCACAACCT TCCACAACCA TCCACAACCA TCCACAACCA TCCACAACCA TCCACAACCA TCCACAACCA TTCCACAACCA TTCCACAACCA TTCCACAACCA TTCCACAACCA TTCCACAACA AACTTACTC TCCACAACCA ACTTCACCAAG ACTTCACCAAG ATTTCCACAAG ATTTCCACAAG ATTTCCACAAG ATTTCACCAAG ATTTCACCAAG ATTTCACCAAG ATTTCACCAAG ATTTCACCAAG ATTTCACCAAG TCCACAACTTG TCCACAACGA TCCACAACTTG TCCACAACGA ACTTCACCAAG ATTTCACCAAG ATTTCACAAAC CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 TACACTAATG ATTTCACAAA AGTAACCAAT TAAACCAAC 2250 TACACTAATG ATTTCATTCA AGTAAACCATT TAAACCAAC GATACACAAC 2300 TACACTAATG ATTTCATCA AGTAAACACTAC AGTACAC	GACTAGIGAG	AMOGINGAMA	CANCTTCCTA	CAGTGGATCC	TGTACAAGAA	1200
TTTAATATG GACGGAACAA TTGAATTATA TTTACCATCA GGAGAAGTCA TTAAAAAGAA TATGGCAGAT TTTACAGGAG AAGCACCTCA AGGAAATGGT 1350 CAACCAACA GAAAATAAAC CAGCAGAATC TTTACCAGAG GCACCAAACG 1450 CAACCAACA GAAAACCAGAA AACCCAGG ATAATGGAAT GTTGAATCA 1500 CAACCAACA GAAAACCAGAA AACCCAGGA ATAATGGAAT GTTGAATCA 1500 CCCTATGTTA GATCCAGCAT TAGAGGAAGC 1550 CCCTATGTTA GATCCAGCAT TAGAGGAAGC 1550 CCCTATGTTA AAGAAAAATT ACAGCTAGTT 1600 ACCGGATTAGG CTTAGATAGA ACGATTGAA 1650 ACGGATTGA CAAGTAGAAAAATT AAACCATGA TCCACAACG ATAATGGAAT CTGATTCAT 1600 ACGGAAGCTT CCACAACCAG CAACCATTG GGTACCAGAT TCCAGACCAG 1750 ACCCACAACC TCCACAACCAG TCCACACACG CTCAACCAGA TCCACACACG TCCAAGCAAT CCAAATGAT ACAGCTAGAT 1800 ACCCATAGAACCATG GTTCCACAACC TCCACACACC TCCACACACC TCCAAGCAAT TCCACACCAG TCCAAGCAAT TCCACACCAG TCCACACACC TCCACACACC TCCAAGCAAT TTTCACCAAG ACTCCAGAAACC TTTTCAGCAGA AACAACCAGC TCCAAGCAAT TTTCAGCAGA AACAGCAGCA 1950 ACCCAAGAAAC TTTTCAGCAGA AACAGCAGCA 1950 ACCCAAGAAAC TTTTCAGCAGA AACAGCAGCA 1950 ACCCAAGAAAC TTTTCAGCAGA AACAGCAGCA 1950 ACCCAAGAATC TTTCAGCAGA AACCAAATGC AACCAAATGC AACCCAAGAATC TTTCAGCAGA AACCAAATGC AACCCAAGAATC TTTTCAGAAC AACCAAATGC AACCCAAATGC AACCAAATG	CTAGTAATTC	AACGIIAGAA	ANGTTATGGG	ATGAAGCTAG	AAAATGTCTT	1250
TTAAAAAGAA TATGGCAGAT TTTACAGGAG AAGCACCTCA AGGAAATGGT 1550 GAAAATAAAC CATCTGAAAA TGGAAAAGTA TCTACTGGAA CAGTTGAGAA 1400 CCAACCAACA GAAAATAAAC CAGCAGATTC TTTACCAGAG GCACCAAACG 1450 AAAAACCTGT AAAACCAGAA AACTCAACGG ATAATGGAAT GTTGAATCCA 1500 GAAGGGAATG TGGGGAGTGA CCCTATGTTA GATCCAGCAT TAGAGGAAGC 1550 TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAATTT ACAATTGAAT 1600 ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA 1650 AGCGAAGCTT CGACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCG 1750 AGCGAAGCTT CCACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCT 1800 GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGATG AGAAATTGGT 1850 GGACTTTCTC GTTCGAAAAG TAGGCGATGG TTTTCAGCAGA AACAGCAGCA 1950 GGCATTGATA GCAAACTGC CAAGCAGGAA AGTTTATCTT GAGGAGAATC TTCAGCAGA 1950 GGCATTGATA ACTGACCAGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG 2000 GGCATTGATA ACTGACCAGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG 2000 CTTATGACTT ACTGACAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT 2050 CTTATGACTT ACTGACAAG ATTCACCAAG ATTTACTTGA TAATAAAGGT 2100 CTCCGAATTCG TTTTGAGCA AGTTAGTGA TCGAAAATT TACAATAAGG 2050 CTCCGATTCG TTTTTGAGCA AGTTAGTGA TGATATTCTT GCCTTATGGAC 2200 CTCCGATTCG TCATCAGAA AGTTAGTGA TGATATTCTT GCCTTCTTAG 2200 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC CTGTTTGGAAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC TGATAATTCT GCCTTCTTAG 2200 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC TGATAATTCT GCCTTCTTAG 2200 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC TGATAATTCT GCCTTCTTAG 2200 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC TGATAATTCC 2250 CTCCGATTCG TCATCCAGAA CTTTTGGATAAC TTTTGGCAGCA AGCCAAATCC 2250 CTCCGATTCG TCATCCAGAA TTTTGGCAA AACCAAATCC GCAAATTACC 2250	AAAGTAGCAA	CACCCAACAA	TTGAATTATA	TTTACCATCA	GGAGAAGTCA	1300
GAAAATAAAC CATCTGAAAA TGGAAAAGTA TCTACTGGAA CAGTTGAGAA CCAACCAACA GAAAATAAAC CAGCAGATTC TTTACCAGAG GCACCAAACG 1450 AAAAACCTGT AAAACCAGAA AACTCAACGG ATAATGGAAT GTTGAATCA 1500 GAAGGGAATG TGGGGAGTGA CCCTATGTTA GATCCAGCAT TAGAGGAAGC 1550 TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAATT AGAAAAATT AGAAAAATT AGAAAAATT AGAAAAATT AGAAAAATT AGAAAAATT ACAGCTAGTT 1600 ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA 1650 AGCGAAGCTT CGTTATCGTT CAAACCATTG GGTACCAGAT TCCAGCAGC 1750 AGGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCGCAACCT 1800 GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGATG AGAAATTGGT 1850 GAGTTTCTCG TTATATCCCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA 1950 GGCATTGATA GCAAACTGGC CAAGCAGAAT TTTCAGCAGA AACAGCAGCA 1950 GGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG 2000 GGCATAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG 2050 CTTATGACTT ACTAGCAGA ATTCACCAAG ATTTACTTGA TAAAACTAGG 2050 CTTATGACTT ACTAGCAGA ACTGACCAG TTTGGATAAC CTGTTGGAAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CTTTGGATAAC CTGTTTGGAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CTTTGGATAAC CTGTTTGGAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CTTTAGGAA AACCAAATCC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CTTTAGCAAG AACCAAATCC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CTTTAGGAA AACCAAATCC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CTTTAGGAA AACCAAATCC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CTTTTAGGAA AACCAAATCC GCAAATTACC 2250 CTCCGATTCG TCATCCTGTG ATCCTCGTGA TATAACCAGT GATGACCAAC 23300	GTTTAALAIG	TATOCCA CAT	TTTACAGGAG	AAGCACCTCA	AGGAAATGGT	1350
CCAACCACA GAAAATAAAC CAGCAGATTC TTTACCAGAG GCACCAAACG AAAAACCTGT AAAACCAGAA AACTCAACGG ATAATGGAAT GTTGAATCCA GAAGGGAATG TGGGGAGTGA CCCTATGTTA GATCCAGCAT TAGAGGAAGC TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAAATT ACAGCTAGTT ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA AGGAACCAAG CAAGCCATTG GGTACCAGAT TCAAGACCAG 1750 AGGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCT 1800 GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGAT GAGAAATTGGT 1850 GAGTTTCTCG TTATATCCCA GCCAAGCAT TTATGTCTTT GAGGAGAATG 1900 GGCATTGATA GCAAACTGGC CAAGCAGGAA ACAGCAGCA 1950 GGCATTGATA ACTAGCAGA ACTCACAAG ATTCACCAAG ACTCACAAG ACTCACAAGCA ACTCACAAG ACCCAAATGC GCAAATTACC CCTCCGATCG TCATCCAGAA ACTCACAAG ACCCAAATGC GCAAATTACC CCTCCGATCG TCATCCAGAA ACCCAAATGC GCAAATTACC CCTCCGATCG TCATCCAGAA ACCCAAATGC GCAAATTACC CCTCCGATCG TCATCCAGAA ACCCAAATGC GCAAATTACC CCTCCCGATCG ACTCACAGA ACCCAAATGC GCAAATTACC CCTCCCGATCG ACTCACAGA ACCCAAATGC GCAAATTACC CCTCCCGATCG ACTCACAGA ACCCAAATGC GCAAATTACC CCTCCCGATCG ACCCACAATTACC CCTCTTAGGAA ACCCAAATGC GCAAATTACC CCTCCCGATCG ACCCACAATTACC CCTCTTAGGAA ACCCAAATGC GCAAATTACC CCTCCCGATCA ACCCAAATGC GCAAATTACC CCTCCCGATCA ACCCAAATGC GCAAATTACC CCTCCCAAGAA ACCCAAATGC GCAAATTACC CCTCCCGTGA ACCCAAATGC GCAAATTACC CCTCCCAACCT TTAGAACACAAC TTGGCAGGA ACCCAAATGC GCAAATTACC CCAAATGC ACCAAATGC GCAAATTACC CCAATGACAAC ACCAAATGC GCAAATTACC CCAAATGCAAC ACCAAATGC GCAAATTACC CCAAATGCAAC ACCAAATGC GAAATTACC CCAAATGCAAC ACCAAATGC GCAAATTACC CCAAATGCAAC ACCAAATGC C		CATCTCANA	тссьььыста	TCTACTGGAA	CAGTTGAGAA	
AAAAACCTGT AAAACCAGAA AACTCAACGG ATAATGGAAT GTTGAATCA GAAGGGAATG TGGGGAGTGA CCCTATGTTA GATCCAGCAT TAGAGGAAGC TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAAATT ACAGCTAGTT ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA AGGAACCATG CAAGTGGAGA AGTGATAAAA AAGAATTTAT CTGATTTCAT AAGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCG TCCAAACCATT GAAACCATTG GCACCAAACCT TCCAAACCAGT TCCAAACCAT TCAAGACCAG TCCAAACCAT TCAAGACCAG TCCAAACCAT TCAAGACCAG TCCAAACCAT TCAAGACCAG TCCAAACCAT TCAAGACCAG TCCAAACCAT TCAAGACCAG TCCAAACAACC TCCAAACCAG TCCAAACAACC TTATATCCCA GCCAAGAAC TTATGTCTTT GAGGAGAAAT TTACAATAAGG TTATATCCCA GCCAAGAACC TTTCAGCAGA AACAGCAGCA 1950 AGCTAAGAAA ACTGACCTCC CAACCAGGAA AGTTTATCTC ATAAGCTAGG 2000 AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAAATT TACAATAAGG 2050 CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT 2100 CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2200 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 CAACACGTT TATATCTTT ATTCCTTTT TTTGAGGCA AGTACACAAC 2300 CTACACTGATT TATATCTTTTT ATTCACTAGA AACCAAATGC GCAAATTACC 2250 CTACACTGATT TATATCTTTTT ATTCACCAAC TTTGGCAGGA AGTACACAAC 2300 CTACACTGATT TATATCTTTTTTTTTTTTTTTTTTTTTT	GAAAATAAAC	CHICIONAN	CAGCAGATTC	TTTACCAGAG	GCACCAAACG	1450
GAAGGGÁATG TGGGGAGTGA CCCTATGTTA GATCCAGCAT TAGAGGAAGC TCCAGCAGTA GATCCTGTAC AAGAAAAATT AGAAAAAATT ACAGCTAGTT ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG AACGATTGAA AGGGAAGCTT CAAGTGGAGA AGTGATAAAA AAGAATTTAT CTGATTTCAT AAGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCACAACCT GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGATG AGAAAATTGGT GAGTTTCTCG TTATATCCCA GCCAAGCAT TTATGTCTTT GAGGAGAATT GGGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG AGCTAAGAAA ACTGACCTCC CATCTAGTGA AGTTTATCTC ATAAGCTAGG CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACCTAAGGA TGTCTCAAGT GATAAAGTCA AGTTAGTGGA AACCAAATGC GCAAATTACC CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGAGT TATATCTTA AGTAGCCAAG TTGGCAGGCA AGTACACAAC TACACTGATG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG TCATCCAGAA CGTTTAGGAA TTGGCAGGCA AGTACACAAC TTGCACTGATT TATATCTTTA AGTAGCCAAG TTGGCAGGCA AGTACACAAC TTGCACTGATT TATATCTTTA AACCAAGT GATGAGGGGG AACCACAACC TTGCACTGATTA TTTTATCTTTA AACCAAC TTGGCAGGCA AGTACACAAC TTGCACTGATTA TTTTTATCTTTATATCTTTATATCTCTTTATATCTCTTTATATCTCTTTATATCTCTTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATCTTTATATCTCTTATATCTCTTATATCTCTTATATCTCTTATATATCTCTTATATCTTATATCTCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTTATATCTATAT	* * * * * * * * * * * * * * * * * * * *	カカカカののかのかれ	AACTCAACGG	ATAATGGAAT	GTTGAATCCA	1500
TCCAGCAGTA ACGATTAGG ACGGATTAGG CTTAGATAGT ACGGATTAGG ACGGATTAGG CTTAGATAGT TTAAGATTGC AGGGAGGA AGTGATAANA AGGATTTAT CTGATTCAT ACAGCCAG AGGGAAGCTT CGTTATCGTT CAAACCATTG GGTACCAGAT TCCAGCACCT ACCACACCG GCACCAAATC CTCAACCAGC CTAGTCCAAG AGAAATTGGT AGGAGAATC CTCAACCAGC CTAGTCCTT GAGGAGAATC ACAACTAGC ACCAAGAACC CCAATTGATC ACAACCAGC AGCTAAGAAA ACTGACCTCC CAACCAGGAA ACTTACTCC ACTAGCAAGA ACTTACTCC CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTTAC	G3 3 GGGZ 3 TYG	TOCOCONCTON	CCCTATGTTA	GATCCAGCAT	TAGAGGAAGC	1550
ACGGATTAGG CTTAGATAGT GTTATATTCA ATATGGATGG ARCGATTGAR TTAAGATTGC CAAGTGGAGA AGTGATAAAA AAGAATTTAT CTGATTTCAT AGCGAAGCTT CGTTATCGTT CAAACCATTG GGTACCAGAT TCAAGACCAG AGCGAAGCT CCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCGCAACCT AAGAACCAAGT CTCAACCAGC TCCAAGCAAT CCCAATTGATG AGAAATTGGT 1850 CAAAGAAGCT GTTCGAAAAG TAGGCGATGG TTATGTCTTT GAGGAGAATG 1900 GGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG 2000 AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG 2050 CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT 2100 CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2200 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC 2300 ACAACAGGT TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	maga act amb	つみずつつではするこ	AAGAAAATT	AGAAAAATII	ACAGCIAGII	1600
TTAAGATTGC CAAGTGGAGA AGTGATAAAA AAGAATTTAT CTGATTCAT AGCGAAGCTT CGTTATCGTT CAAACCATTG GGTACCAGAT TCAAGACCAG 1750 AAGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCGCAACCT 1800 GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGATG AGAAATTGGT 1850 CAAAGAAGCT GTTCGAAAAG TAGGCGATGG TTATGTCTTT GAGGAGAATG 1900 GAGTTTCTCG TTATATCCCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA 1950 GGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG 2000 AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG 2050 CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT 2100 CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA 2150 CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2200 TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC 2300 TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC 2300 TACACTGATG TTATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	* こここ かかがかごう	CTTAGATAGT	GTTATATTCA	ATATGGATGG	AACGALIGAA	1650
AGCGAAGCTT CGTTATCGTT CAAACCATTG GGTACCAGAT TCAGACACAG AAGAACCAAG TCCACAACCG ACTCCAGAAC CTAGTCCAAG TCCGCAACCT GCACCAAATC CTCAACCAGC TCCAAGCAAT CCAATTGATG AGAAATTGGT CAAAGAAGCT GTTCGAAAAG TAGGCGATGG TTATGTCTTT GAGGAGAATG GAGTTTCTCG TTATATCCCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA AGCTAAGAAA ACTGACCTCC CAAGCAGGAA AGTTTATCTC ATAAAGCTAGG CGTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA CGTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC TACACTGATG TTATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG ACTCACGGT TATATCTTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 1800 1	MADE & CROSSOCIO	CANCTCCAGA	AGTGATAAAA	AAGAATTTAT	CIGATITCAL	_
AAGAACCAAG GCACCAAACC GCACCAAACC GCACCAAACC GCACCAAACC GCACCAAACC CTCAACCAGC TCCAAGCAAT CCCAATTGATG AGAAATTGGT 1850 CAAAGAAGCT GTTCGAAAAG TAGGCGATGG TTATGTCTTT GAGGAGAAT 1900 GGCATTGATA GCAAACTGGC CAAGCAGGAA ACTGCACCA GGCAAGAATC TTCAGCAGA ACTGACCTC CATCTAGTGA CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC CTGTTGGAAC CTGTTGGACC CTGTTGGACC CTGTTGGACC CTGTTCAAGT CTCCGATTCG TCATCCAGAA CGTTTAGGAA ACCAAATGC CCACTTATGC CTCCGATTCG TCATCCAGAA CGTTTAGGAA ACCAAATGC CGCACAACC CCCATTTAGGAA CCCATTTAGCACC CTGTTGGAAC CGCTTCTTAG CCCTTCTTAG CCCACTCC CCCACTCC CCCACTCC CTGTTGGACC CTGTTGGACC CCCTTCTTAG CCCTTCTTAG CCCTTCTTAG CCCTTCTTAG CCCTTCTTAG CCCACTCC CCCACTCC CCCCACTCC CTCCGATTCC CTCCGATTCC CTCCGATTCC CTCCGATTCC CTCCGATTCC CTCCCGTTCT CCCACTCC CCCACTCCT CCCACTCC CCCACTCCT CCCACTCC CCCACTCCT CCCACTCC CCCACTCCT CCCACTCCT CCCACTCCT CCCACTCC CCCACTCCT CCCACTCC CCCCCCC CCCACTCCT CCCACTCC CCCCCCC CCCCCCC CCCCCCCC	NOOD BOOT	COTTANTCATT	CABACCATTG	GGTACCAGAT	TCAAGACCAG	
CAAAGAATC CAAACAAGC CAAAGAAGC CAAGCAGGAA CCCCCCCC		TOURCARCE	ACTCCAGAAC	CTAGTCCAAG	TUCGUAACUI	
CAAAGAAGCT GTTCGAAAAG TAGGCGATGG TTATGTCTTT GAGGAGAATC GAGTTTCTCG TTATATCCCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA GGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA CGACAAGTTG GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTTAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC AGTAGCCAAG TTTGGCAGGCA AGTACACAAC AACACACGC GATGAGGGG AACTACACAC 2300 TACACTGATG TTATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	GONGON NATO	CTCDACCAGC	TCCAAGCAAT	CCAATIGATG	AGWAMIIGGI	
GAGTTTCTCG TTATATCCCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA GCCAAGAATC TTTCAGCAGA AACAGCAGCA AACAGCAGCA GCCAAGATTCACAGA AACAGCAGCA AACAGCAGCA AACAGCAGCA AACAGCAGCA AACAGCAGCA AACAGCAGCA AACAGCAGCA AACAGCAAGA ACTAAGAAAAAAAAAA	OB 3 5 O 5 3 C C C	CTTCCAAAAG	TAGGCGATGG	TTATGTCTTT	GAGGAGAATG	
GGCATTGATA GCAAACTGGC CAAGCAGGAA AGTTTATCTC ATAAGCTAGG AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTT TACAATAAGG CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTTGGATAAC CTGTTGGAAC GACTCAAGGA TGTCTCAAGT GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTTAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC TACACTGATG TTATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2050 2050 2050 2050 2050 2050 2050	ON COMPUTATION	ጥጥልጥልጥርርሮል	GCCAAGAATC	TTTCAGCAGA	AACAGCAGCA	
AGCTAAGAAA ACTGACCTCC CATCTAGTGA TCGAGAATTI TACAATAAGG CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTGGATAAC CTGTTGGAAC GACTCAAGGA CGTCTCAAGT GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTTAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC TACACTGATG TTATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	A A A A TOTAL A TO	CCAAACTGGC	· CAAGCAGGAA	AGTTTATCIC	ATAAGCTAGG	
CTTATGACTT ACTAGCAAGA ATTCACCAAG ATTTACTTGA TAATAAAGGT CGACAAGTTG ATTTTGAGGC TTTGGATAAC CTGTTGGAAC GACTCAAGGA TGTCTCAAGT GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTTAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTTGGCAGGCA AGTACACAAC TACACTGATG TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	አመመሞ አለር አለ አ	ACTGACCTCC	· CATCTAGTGA	TCGAGAATTI	TACAATAAGG	
CGACAAGTTG ATTTTGAGGC TTTGGATAAC CTGTTGGAAC GACTCAAGGA TGTCTCAAGT GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTTAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC AGTAGCCAGT TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	COMPANY OF A COMPA	NOTAGENAGE	ATTCACCAAG	ATTTACTIGA	TAATAAAGGI	
TGTCTCAAGT GATAAAGTCA AGTTAGTGGA TGATATTCTT GCCTTCTIAG CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC AGTAGCCAGG TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	CONCANTITO	ስጋጋር ልጋም ምጥ ለ	TTTGGATAAC	CTGTTGGAAC	GACTCAMGGA	
CTCCGATTCG TCATCCAGAA CGTTTAGGAA AACCAAATGC GCAAATTACC 2250 TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC 2300 AGAACACGGT TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	mamara N N CT	CATABACTC	AGTTAGTGG	TGATATICII	GCCTTCTTWG	
TACACTGATG ATGAGATTCA AGTAGCCAAG TTGGCAGGCA AGTACACAAC 2500 AGACACGGT TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGGG 2350	CONCCC NIPTEC	TOATCCAGAI	L CGTTTAGGA	AACCAAATGU	GCAAAIIACC	
AGAGAGGGT TATATCTTTG ATCCTCGTGA TATAACCAGT GATGAGGGG 2350	MACACTICATO	: አጥርልርል ጥ ጥር	AGTAGCCAA(3 TIGGCAGGLA	AGIACACAAC	
ATGCCTATGT AACTCCACAT ATGACCCATA GCCACTGGAT TAAAAAAGAT 2400	NONACACIGG	TATATCTTT	: ATCCTCGTGA	A TATAACCAGI	GATGAGGGGG	
	ATGCCTATGT	AACTCCACAT	r atgacccati	A GCCACTGGAT	TAAAAAAAGAT	2400

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AMENDED SHEET __

	*********	AGCGGCAGCC	CAGGCTTATG	CTAAAGAGAA	2450
AGTTTGTCTG	AAGCIGAGAG	AGCGGCAGCG	CCATTCAGGA	AATACTGAGG	2500
AGGTTTGACC	CCTCCTTCGA	CAGACCATCA	GGATICAGGA	manda addTC	2550
CAAAAGGAGC	AGAAGCTATC	TACAACCGCG	TGAAAGCAGC	TAAGAAGGIG	
CONCETTENTO	GTATGCCTTA	CAATCTTCAA	TATACTGTAG	AAGTCAAAAA	2600
CCACITORIO	አጥሮአጥአርርጥር	ATTATGACCA	TTACCATAAC	ATCAAATTTG	2650
CGGTAGTTIA	WICHINCOIC	TATGAGGCAC	CTAAGGGGTA	TACTCTTGAG	2700
AGTGGTTTGA	CGAAGGCCTT	TATGAGGCAC	CINCOCCI.	ACCAACGTCC	2750
GATCTTTTGG	CGACTGTCAA	GTACTATGTC	GAACAICCAA	ACGAACGICC	2800
CONTTCAGAT	AATGGTTTTG	GTAACGCTAG	CGACCATGTT	CAAAGAAACA	
A A A A A A A A COUNCY	ACCTCATACC	AATCAAACGG	AAAAACCAAG	CGAGGAGAAA	2850
AAAAIGGICA	AGCIGATACC	CONNCANNCC	CCTCGAGAAG	AGAAACCACA	2900
CCTCAGACAG	AAAAACCIGA	GGAAGAAACC	ACT CONTROL	GAAGAAGAAT	2950
AAGCGAGAAA	CCAGAGTCTC	CAAAACCAAC	AGAGGAACCA	CAMOUNTAINA	3000
CACCAGAGGA	ATCAGAAGAA	CCTCAGGTCG	AGACTGAAAA	GGTTGAAGAA	•
BARCTCACAC	AGGCTGAAGA	TTTACTTGGA	AAAATCCAGG	ATCCAATTAT	3050
AMACIGAGAO	CCCAAACACA	CTCTCACAGG	TAAAAAAT	AATITACTAT	3100
CAAGTCCAAT	GCCARAGAGA	CICICACATO	CACAAGCTGA	AAAACTATTG	3150
			CHOMMOCION	AAAACTATTG	3171
GCTTTATTAA	AGGAGAGTAA	G (SEQ I	D NO : 76)		21.1

EAYWNGKQGS RPSSSSSYNA	MOVODRISEN	HNLTVTPTYH	QNQGENISSL	50
LRELYAKPLS ERHVESDGLI	TODA OTTODT	ARGUAVEHGN	HYHFIPYEOM	100
LRELYAKPLS ERHVESDGLI	FDPAQIISKI	POCEDEDEDE DE	TODA DNDODA	150
SELEKRIARI IPLRYRSNHW	VPDSRPEQPS	PUSIPERSTS	TANCIDERI'Y	200
PSNPIDEKLV KEAVRKVGDG	YVFEENGVSR	YIPAKULSAE	TAAGIDSADA	250
WORDT CHELC ARREDT DEED	REFYNKAYDL	LARIHQDLLD	NKGKOADLEA	300
TOULTEDIAN VSSDKVKLVD	DILAFLAPIR	HPERLGRPNA	OTLITABLETO	
TIREL NOWWEL EDGALEDED	TTSDEGDAYV	TPHMTHSHWI	KKDSDSEMEK	350
ANANYAVEV GLTDDSTDHO	DSGNTEAKGA	EALYNRVKAA	KKAAPDKMAI	400 -
NLQYTVEVKN GSLIIPHYDH	VHNIKEEWED	EGLYEAPKGY	SLEDLLATVK	450
MPGALARAKU GSPITEHIDU	DUN (CEO	ID NO : 77		473
YYVEHPNERP HSDNGFGNAS	DWA (SEA	10 1.0	•	

FIGURE 42

CAYALNQHRS	QENKDNNRVS	YVDGSQSSQK	SENLTPDQVS	QKEGIQAEQI	50
VIKITDQGYV	TSHGDHYHYY	NGKVPYDALF	SEELLMKDPN	YQLKDADIVN	100
EVKGGYIIKV	DGKYYVYLKD	'AAHADNVRTK	DEINRQKQEH	VKDNEKVNSN	150
VAVARSQGRY	TTNDGYVFNP	ADIIEDTGNA	YIVPHGGHYH	YIPKSDLSAS	200
ELAAAKAHLA	GKNMQPSQLS	YSSTASDNNT	QSVAKGSTSK	PANKSENLQS	250
LLKELYDSPS	AQRYSESDGL	VFDPAKIISR	TPNGVAIPHG	DHYHFIPYSK	300
LSALEEKIAR	MVPISGTGST	VSTNAKPNEV	VSSLGSLSSN	PSSLTTSKEL	350
SSASDGYIFN	PKDIVEETAT	AYIVRHGDHF	HYIPKSNQIG	QPTLPNNSLA	400
TPSPSLPINP	GTSHEKHEED	GYGFDANRII	AEDESGFVMS	HGDHNHYFFK	450
KDLTEEQIKA	AQKHLEEVKT	SHNGLDSLSS	HEQDYPGNAK	EMKDLDKKIE	500
EKIAGIMKQY	GVKRESIVVN	KEKNAIIYPH	GDHHHADPID	EHKPVGIGHS	550
HSNYELFKPE	EGVAKKEGNK	VYTGEELTNV	VNLLKNSTFN	NONFTLANGO	600
KRVSFSFPPE	LEKKLGINML	VKLITPDGKV	LEKVSGKVFG	EGVGNIANFE	650
LDQPYLPGQT	FKYTIASKDY	PEVSYDGTFT	VPTSLAYKMA	SQTIFYPFHA	700
GDTYLRVNPQ	FAVPKGTDAL	VRVFDEFHGN	AYLENNYKVG	EIKLPIPKLN	750
QGTTRTAGNK	IPVTFMANAY	LDNQSTYIVE	(SEQ ID)	NO : 78)	780
			FIGURE 4	3	
	•	YIDGKQATQK		-	50.
		NGKVPYDAII			100
		AAHADNVRTK		-	150
		IFNASDIIED			200
		NLRTYRRQNS			250
		LTKÖTAKT br			300
		MSELEKRIAR			350
· · •		APSNPIDEKL			400
		AKQESLSHKL			450
-		ALDNLLERLK			500
		QVAKLAGKYT			550
		RAAAQAYAKE		-	600
		YNLQYTVEVK		HYHNIKFEWF	650
		KYYVEHPNER	PHSDNGFGNA		690
(SEQ ID NO	: 79)				

GTGAAGAAAA	CATATGGTTA	TATCGGCTCA	GTTGCTGCCA	TTTTACTAGC	TACTCATATT	60
CONSCITATION	ስ ልርጥፕፕሮርጥል ል	GCATCATATG	GGTCTAGCAA	CANAGGACAA	ICHONITOCC	120
DT 6 SYPTI 6 TO 6 TO	ACACCAAAGG	TAAGGCAAAA	GCCCCTAAAA	CAAACAAAAC	GATGGATCAA	180
NTC NOTOCTC	AAGAAGCAT	CTCTGCTGAA	CAGATCGTAG	TCAAAATTAC	TGACCAAGGC	240
ምአምር ጥር እ ርርጥ	CACACGGTGA	CCATTATCAT	TTTTACAATG	GGAAAGTTCC	TTATGATGCG	300
አምምአምምልርጥር	AACAGTTGTT	GATGACGGAT	CCTAATTACC	GTTTTAAACA	ATCAGACGII	360
A C A SYPA A DYA	TCTTAGACGG	TTACGTTATT	AAAGTCAATG	GCAACTATTA	IGITIACCIC	420
AACCCACCTA	GTANGCGCAA	AAACATTCGA	ACCAAACAAC	AAATTGCTGA	GCAAGTAGCC	480
222C22CT2	አአርአአርርፕልአ	DGAAAAGGT	TTAGCTCAAG	TGGCCCATCT	CAGIAAAGAA	540
CARCTTCCCC	CAGTCAATGA	AGCAAAAAGA	CAAGGACGCT	ATACTACAGA	CGAIGGCIAI	600
A TOTO TOTO TOTO	CGACAGATAT	CATTGATGAT	TTAGGAGATG	CTTATTTAGT	ACCICATGGI	660
N N TO A COTTA TO	እጥጥ ለጥ ለጥጥርር	TADDAAAAT	TTGTCTCCAA	GTGAGCTAGC	IGCIGCACAA	720
CCCTACTCCA	GTCDADAGA	AGGTCGAGGT	GCTAGACCGT	CTGATTACCG	CCCGACACCA	780
CCCCCACCTC	CTACCAAACC	CCCAATTCCT	GATGTGACGC	CTAACCCTGG	ACAAGGICAI	840
CACCCACATA	ACCCTCCCTA	TCATCCAGCG	CCTCCTAGGC	CAAATGATGC	GICHCHAMAC	900
*******	CACATCACTT	TAAAGGAAAA	ACCTTTAAGG	AACTITIAGA	TCAACTACAC	960
CONCINTONT	TONDATACCG	TCATGTGGAA	GAAGATGGGT	TGATTTTTGA	ACCGACTCAA	1020
COUCA TOTAL AT	CAAACGCTTT	TCCCTATGTG	GTGCCTCATG	GAGATCATTA	TCATATTATC	1080
CONNONNOTO	ACTTN TCACC	TCTTCAAATG	GAATTAGCAG	ATCGATACTT	AGCIGGCCAA	1140
NOTED COLCD	ATCACTCAGG	TTCAGAGCAC	TCAAAACCAT	CAGATAAAGA	AGIGACACAI	1200
P COLUMNICAL CALACITY	GTCATCGCAT	CARAGCTTAC	GGAAAAGGCT	TAGATGGTAA	ACCATATGAT	1260
A CONCERCTO	ለተምተለጥረታም ተ	TAGTAAAAAAA	TCCATTCATT	CAGTGGATAA	ATCAGGAGII	1320
A CACCOTA NAC	ACCOAGATCA	TTTCCACTAT	ATAGGATTTG	GAGAACTIGA	ACAATATGAG	1380
TTCCTTCTCC	ጥርያርሞልልርፕር	GGTGAAAGCA	AAAGGTCAAG	CTGATGAGCT	TUCTUCTUCT	1440
TTCCATCAGG	AACAAGGCAA	AGDAAAACCA	CTCTTTGACA	CTAAAAAAAGT	GAGTCGCAAA	1500
CTABCABAAG	TOGGTAAAGT	GGGCTATATG	ATGCCAAAAG	ATGGTAAGGA	CIATITCIAL	1560
COMCOMONTO	እ አርጥጥር <u>አጥ</u> ጥጥ	GACTCAGATT	GCCTTTGCCG	AACAAGAACT	AAIGCIIAAA	1620
CATARCARCC	ልጥተል ርርርር ተዋል	TGACATTGTT	GACACAGGTA	TIGAGCCACG	ACTIGCIGIA	1680
CATCITCITCA	CTCTGCCGAT	GCATGCTGGT	AATGCTACTT	ACGATACTGG	AAGTICGIII	1740
COMPATICICA C	ለጥለ ጥጥር እጥር ል	TATCCATGTC	GTTCCGTATT	CATGGTTGAC	GCGCGATCAG	1800
*************************************	TONDOTATOT	GATGCAACAC	CCCGAAGTTC	GTCCGGATGT	AIGGICIAAG	1860
CONCCCCNTC	AACACTCAGG	TTCGGTCATT	CCAAATGTTA	CGCCTCTTGA	TAAACGIGCI	1920
COMP TO CO A	አርጥርርር D D D T	TATCCATTCT	GCTGAAGAAG	TTCAAAAAGC	CCTAGCAGAA	1980
ACTOC TOTOL	CARCACCAGA	CGGCTATATT	TTCGATCCAC	GAGATGTTT	GGCCAAAGAA	2040
* Communicates at	CONNAGATOO	CTCCTTTAGC	ATCCCAAGAG	CAGATGGCAG	TICALIGAGA	2100
አ ር/ር እ የምኒስ '\ የኒስ	እ እጥርጥር እጥር ጥ	ATCCCAAGCT	GAGTGGCAAC	AAGCTCAAGA	GTTATTGGCA	2160
**********	CTCCTCATCC	TACTGATACG	GATAAACCCA	AAGAAAAGCA	ACAGGCAGAI	2220 2280
>> C > C C C C > T C C	*********	CCCAACTGAA	GCCAGTAAAG	AAGAAAAAGA	ATCAGATGAC	
THE PROPERTY OF THE PROPERTY O	GTTTACCAGA	CTATGGTCTA	CATAGAGCAA	CCCTAGAAGA	TUMINICAMI	2400
CAN A COMPA COMPA CO	ፈል ተ ግርካል ለፈለፈ	TATCGATCCT	· AAGTATCTCA	TTTTCCAACC	AGMAGGIGIC	2400
CAATTTTATA	ATAAAAATGG	TGAATTGGTA	ACTTATGATA	TCAAGACACT	TCAACAAATA	2469
AACCCTTAA	(SEQ ID N	0 : 80)				2403

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VKKTYGYIGS VAAILLATHI	GSYQLGKHHM	GLATKDNQIA	YIDDSKGKAK	50
APKTNKTMDQ ISAEEGISAE	QIVVKITDQG	YVTSHGDHYH	FYNGKVPYDA	100
IISEELLMTD PNYRFKQSDV	INEILDGYVI	KVNGNYYVYL	KPGSKRKNIR	150
TKQQIAEQVA KGTKEAKEKG	LAQVAHLSKE	EVAAVNEAKR	QGRYTTDDGY	200
IFSPTDIIDD LGDAYLVPHG	NHYHYIPKKD	LSPSELAAAQ	AYWSQKQGRG	250
ARPSDYRPTP APGRRKAPIP	DVTPNPGQGH	QPDNGGYHPA	PPRPNDASQN	300
KHQRDEFKGK TFKELLDQLH	RLDLKYRHVE	EDGLIFEPTQ	VIKSNAFGYV	350
VPHGDHYHII PRSQLSPLEM	ELADRYLAGQ	TEDNDSGSEH	SKPSDKEVTH	400
TFLGHRIKAY GKGLDGKPYD	TSDAYVFSKE	SIHSVDKSGV	TAKHGDHFHY	450
IGFGELEQYE LDEVANWVKA	KGQADELAAA	LDQEQGKEKP	LFDTKKVSRK	500
VTKDGKVGYM MPKDGKDYFY	ARDQLDLTQI	AFAEQELMLK	DKKHYRYDIV	550
DTGIEPRLAV DVSSLPMHAG	NATYDTGSSF	VIPHIDHIHV	VPYSWLTRDQ	600
IATVKYVMQH PEVRPDVWSK	PGHEESGSVI	PNVTPLDKRA	GMPNWQIIHS	650
AEEVQKALAE GRFATPDGYI	FDPRDVLAKE	TFVWKDGSFS	IPRADGSSLR	700
TINKSDLSQA EWQQAQELLA	KKNTGDATDT	DKPKEKQQAD	KSNENQQPSE	750
ASKEEKESDD FIDSLPDYGL	DRATLEDHIN	QLAQKANIDP	KYLIFQPEGV	800
QFYNKNGELV TYDIKTLQQI	NPP (SEQ	ID NO : B1)		823

GTGAAGAAA CATATGGTTA TATCGGCTCA	GTTGCTGCCA	TTTTACTAGC	TACTCATATT	60
CONNECTED ARCTICCTAN CONTOCTATATG	GGTCTAGCAA	CAAAGGACAA	TCHGHIIGCC	120
TARGECAAAA	GCCCCTAAAA	CAAACAAAAC	GATGGATCAA	180
ATCACTCCTG AAGAAGGCAT CTCTGCTGAA	CAGATCGTAG	TCAAAATTAC	TGACCAAGGI	240
TATTATCAT	TTTTACAATG	GGAAAGTTCC	TTATGATGCG	300
AMENDED AND ATTOTT GATGACGGAT	CCTAATTACC	ATTTTAAACA	ATCAGACGII	360
ATTORNESS TOTTAGACGG TTACGTTATT	AAAGTCAATG	GCAACTATTA	TGTTTACCTC	420
PROCESCOTA CTRRCCCCAR ARRCATTCGA	ACCAAACAAC	AAATIGCIGA	GCAAGTAGCC	480
ANACORACCA ANGANGCTAN AGANANAGGT	TTAGCTCAAG	TGGCCCATCT	CAGTAAAGAA	540
CARGOTTOCCO CAGTONATON AGCANANGA	CAAGGACGCT	ATACTACAGA	CGAIGGCIAI	600
ATTEMPTACE CONCOUNTAT CATTGATGAT	TTAGGAGACG	CTTATTTAGT	ACCICATOGI	660
AND CONTROL ATTATATTCC TAAAAAAGAT	TTGTCTCCAA	GTGAGCTAGC	ICCICACAN	720
COMPACTORA GTCAAAACA AGGTCGAGGT	GCTAGACCGT	CTGATTACCG	CCCGACACCA	780
CCCCCACCTC GTAGGAAAGC TCCAATTCCT	GATGTGACGC	CTAACCCTGG	ACAAGGICAI	840
CROCCEONER ACCOMMOND TOATCOAGCG	CCTCCTAGGC	CAAATGATGC	GICACAAAAC	900
AAACACCAAA GAGATGAGTT TAAAGGAAAA	ACCTTTAAGG	AACTTTTAGA	TCAACTACAC	960
CGTCTTGATT TGAAATACCG TCATGTGGAA	GAAGATGGGT	TGATTTTTGA	ACCGACTCAA	. 1020
CTCATCANAT CANACCCTTT TGGGTATGTG	GTGCCTCATG	GAGATCATTA	TCATATTATC	1080
CONNONNEUR ACTIVATEDE TETTGARATG	GAATTAGCAG	ATCGATACTT	AGCCGGTCAA	1140
A CHICAGA CAN A TICATTUAGG TTUAGATUAC	TCAAAACCAT	CAGATAAAGA	AGTGACACAT	1200
ACCOUNT CATTLE CATCATCGCAT CAAAGCTTAC	GGAAAAGGCT	TAGATGGTAA	ACCATATGAL	1260
ACCRETATE CTTATETTT TAGTAAAGAA	TCCATTCATT	CAGTGGATAA	ATCAGGAGII	1320
TO THE TOTAL PROPERTY OF THE COURT OF THE CO	ATAGGATTTG	GAGAACTIGA	ACAATAIGAG	1380
THE CAMERAGE TECCTARCTC GGTGARAGCA	AAAGGTCAAG	CTGATGAGCT	1661661661	1440
THE CANCEL BACABCCCA AGAAAACCA	CTCTTTGACA	CTAAAAAAGT	GAGICGCAAA	.1500
GENERAL AND AUGUTABACT GGGCTATATT	ATGCCAAAAG	ATGGCAAGGA	CIMILICIAL	1560
COMPONENTS ANOTHER GACTCAGATT	GCCTTTGCCG	AACAAGAACT	AAIGCIIAAA	1620
CARACAACC ATTACCCTTA TGACATTGTT	GACACAGGTA	TTGAGCCACG	ACTIGCIGIA	1680
CARGROTTONA CTCTGCCGAT GCATGCTGGT	AATGCTACTT	ACGATACTGG	AAGTICGIII	1740
COMPRESSED ATATTGATCA TATCCATGTC	GTTCCGTATT	CATGGTTGAC	GCGCGATCAG	1800
NUMBER OF THE PROPERTY OF THE CATGORAGE	CCCGAAGTTC	GTCCAGATGT	ATGGTCTAAG	1860
CONCOUNTS ANGMOTORG TICGGTCATT	CCAAATGTTA	CGCCTCTTGA	TAMACGIGCI	1920
COMPARCIONA ATTRICCADAT CATCCATTCT	GCTGAAGAAG	TTCAAAAAGC	CCTAGCAGAA	1980
COMPONENTS CARCACOGA CCCCTATATT	TTCGATCCAC	GAGATGTTTT	GGCCAAAGAA	2040
* COMMONDATAT CONNICATED CTCCTTTAGC	ATCCCAAGAG	CAGATGGCAG	IICAIIGAGA	2100
A COLUMN ACT A PROTONTOT ATCCCAAGCT	GAGTGGCAAC	AAGCTCAAGA	GIIMIIGGCA	2160
TARREST OF COMPANY OF TARREST ATARREST	CATAAACCCA	AAGAAAAGCA	MCMOGCAGAI	2220
	CCCAGTAAAG	AAGAAGAAA	MOMETONONI	2280
GROWSPARAC ACROTTACC AGACTATGGT	CTAGATAGAG	CAACCCIAGA	MONICHIAIC	2340
PARCANTAC CACAAAACC TAATATCGAT	CCTAAGTATC	TCATTTTCCA	ACCHGMAGGI	2.00
GTCCAATITT ATAATAAAAA TGGTGAATTA	GTAACTTATG	ATATCAAGAC	GCTTCAACAA	2460
ATAAACCCTT AA (SEQ ID NO : 82)				2472

ATAAACCCTT AA (SEQ ID NO : 82)

VKKTYGYTGS	VAAILLATHI	GSYOLGKHHM	GLATKDNQIA	YIDDSKGKAK	50
		QIVVKITDQG			100
IISEELLMTD	PNYHFKOSDV	INEILDGYVI	KVNGNYYVYL	KPGSKRKNIR	150
	KGTKEAKEKG	LAOVAHLSKE	EVAAVNEAKR	QGRYTTDDGY	200
	LGDAYLVPHG	NHYHYIPKKD	LSPSELAAAQ	AYWSQKQGRG	250
	APGRRKAPIP	DVTPNPGQGH	QPDNGGYHPA	PPRPNDASQN	300
	TFKELLDQLH	RLDLKYRHVE	EDGLIFEPTQ	VIKSNAFGYV	350
	PRSQLSPLEM	ELADRYLAGQ	TEDNDSGSDH	SKPSDKEVTH	400
	GKGLDGKPYD	TSDAYVFSKE	SIHSVDKSGV		450
	LDEVANWVKA	KGQADELAAA			500
	MPKDGKDYFY	ARDQLDLTQI	AFAEQELMLK	DKNHYRYDIV	550
	DVSSLPMHAG	NATYDTGSSF	VIPHIDHIHV	VPYSWLTRDQ	600
	PEVRPDVWSK	PGHEESGSVI	PNVTPLDKRA	GMPNWQIIHS	650
	GRFATPDGYI	FDPRDVLAKE	TFVWKDGSFS	IPRADGSSLR	700
		KKNAGDATDT	DKPKEKQQAD	KSNENQQPSE	750
ASKEEEKESD		LDRATLEDHI		PKYLIFQPEG	800
	VTYDIKTLQQ	INPP (SE	2 ID NO : 83	3)	824

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